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ORIGINAL ARTICLE

Anxiety and depression among caregivers of young children with Congenital Zika Syndrome in Brazil

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ABSTRACT

Purpose: To examine the psychological well-being of primary caregivers of infants and toddlers with Congenital Zika Syndrome (CZS), and the roles of family resources, parenting stress, and coping strategies in caregivers' adaptation.

Materials and methods: Family caregivers ($N = 50$) of children with CZS who were receiving treatment at a rehabilitation hospital in Recife, Brazil participated a cross-sectional survey study. Caregivers completed measures of anxiety and depression, coping strategies, family resources, and parenting stress.

Results: Mild to severe symptoms of depression were identified in 40% of caregivers and were a more prominent concern than symptoms of anxiety. Fewer family resources and high levels of parenting stress were significantly associated with both anxiety and depression. The association between parenting stress and depression was moderated by coping, such that parenting stress was associated with higher caregiver depression at low but not high levels of coping strategy use.

Conclusions: Practitioners in Brazil should consider the role of family coping and resources as important resilience promoting factors in the development of new programs designed to promote psychological adaptation in caregivers to children with CZS. It is recommended that caregiver mental health support services be integrated into existing early intervention programs targeting children with CZS.

➤ **IMPLICATIONS FOR REHABILITATION**
- Parents and other primary caregivers are encouraged to take an active role in the care and developmental monitoring of children born with CZS, but their ability to provide care may be compromised by difficulties in psychological adaptation.
- Moderate and severe symptoms of depression were more prominent in caregivers than moderate and severe symptoms of anxiety (20% versus 6%, respectively).
- Practitioners should include assessment of coping strategies, parenting stress and family resources conjointly with evaluation of symptoms of depression and anxiety as part of routine CZS family evaluations.
- A useful approach for caregivers in Brazil may be to more fully integrate caregiver mental health support services into existing early intervention programs for children with CZS.

Introduction

On 1 February 2016, the World Health Organization declared an international public health emergency in response to the proliferation of the Zika virus. At that time, active transmission of Zika was reported in 28 countries and territories, with the majority of cases occurring in the Americas, including Brazil, Colombia, Venezuela, Mexico, Haiti, and Barbados. No country was more affected by this outbreak than Brazil, where widespread transmission of this disease was first recognized in 2014 [1]. While most people infected by the Zika virus are asymptomatic or experience only mild symptoms, intrauterine infection can have devastating consequences for fetal development. Zika infection during pregnancy is associated with the occurrence of Congenital Zika Syndrome (CZS), a pattern of congenital anomalies that includes microcephaly and other serious brain abnormalities and sensory

impairments [2–11]. Evidence suggests that pregnant women infected by the Zika virus in early pregnancy are at greater risk of having an infant with microcephaly [2]. A total of 3332 confirmed cases of CZS have been reported in Brazil from 2015 to 1 February 2019, with 70% of cases occurring in the northeast region of the country [12].

Recommended clinical care of infants with CZS includes comprehensive postnatal physical and neurological examination, followed by ongoing monitoring and screening of vision, hearing, feeding, growth, and neurodevelopmental and endocrine functioning [13,14]. Early monitoring and identification of developmental delays is critical to ensure that children receive appropriate subspecialty care, such as speech, visual, occupational, and physical therapies. These services are essential to maximize children's physical and intellectual abilities, and to promote

their participation in family and community life and improve their overall quality of life. Parents and other primary caregivers are encouraged to take an active role in the care and developmental monitoring of children born with CZS [13], and are viewed by the medical team as key partners in providing ongoing developmental stimulation of these young children in the home environment. However, caregivers' capacity to function effectively in this role may be affected by their own emotional state. Psychological distress, particularly symptoms of anxiety and depression, has been shown to compromise parents' coping resources, diminish parent–child relationship quality, and adversely affect parents' ability to problem-solve to meet their child's needs [15,16].

Research on parenting children with complex medical needs raises concerns regarding the impact of caring for a child with CZS on caregivers' psychological well-being. The birth of a child with significant cognitive and physical disabilities presents major challenges and often precipitates family stress [17–20]. Challenges associated with caring for a child with CZS include difficulties related to the developmental and behavioral sequelae of this condition (e.g., high pitched cry, feeding difficulties caused by problems with swallowing and frequent choking, epileptic seizures, muscle stiffness, hyperactivity, visual and auditory impairments, and microcephaly associated with severe developmental delay, intellectual disability), excessive caretaking demands, financial burden, social stigma, difficulties with transportation to reach treatment centers, child mobility challenges, disruption of family functioning and activities of daily living in order to meet the child's needs, and a strained or terminated romantic relationship of the child's parents [14,21–23]. The negative psychological impact of these challenges may be exacerbated among socioeconomically disadvantaged families in Brazil who bore a disproportionate burden of CZS [24].

Guidelines for identifying appropriate services and supports for infants with CZS specify ongoing psychosocial assessment, as well as a family-centered, individualized approach for the provision of services and identification of both formal and informal supports for caregivers and families [13,21]. However, few published studies have documented these caregivers' psychological functioning and needs. Focusing on caregiver psychological adjustment is important for child development and outcomes, and is aligned with a stated global priority of making psychological support services more accessible to caregivers of children with developmental delays and disabilities [25]. This directive is based on the vast literature showing that parental psychological problems such as depression interfere with the provision of sensitive and responsive parenting behaviors, placing children at risk for a range of adverse outcomes including diminished social competence and emotional and behavioral self-regulatory difficulties [26,27]. Of particular relevance to this population, maternal depression can also interfere with caregivers' capacity to acquire child intervention and/or medical services, further compromising children's health and developmental outcomes [15].

Initial studies exploring psychological adaptation in caregivers to children with CZS found that mothers of newborns with microcephaly reported lower psychological quality of life at baseline compared to mothers with healthy newborns [28], and their anxiety symptoms increased from birth to 12 months [29]. It is important to note that there were no significant differences in reported anxiety or depression at birth. More recently, de Souza et al. assessed general mental health, positive and negative affect, fatigue, and life satisfaction in 86 parents of children ages 1–20 months with CZS (M age = 9.67 months) [30]. Almost a fifth (18.6%) of these parents indicated a negative evaluation of their mental health, and nearly 7% had a score indicating poor mental health and probable emotional disorders. In multivariate models, mental health was predicted by less positive and more negative affect, lower life satisfaction, and more fatigue [30]. Little is known regarding the psychological well-being of caregivers to these children beyond infancy, but available evidence is suggestive of persistent mental health concerns for caregivers during the toddler years. In a recently published study, 18% of caregivers to toddlers with congenital Zika virus infection were identified as having moderately severe or severe depressive symptoms [31].

The extant research highlights the importance of evaluating the psychological functioning of caregivers to children with CZS. In particular, there is need to further document the mental health needs of caregivers beyond infancy, as caregiving experiences and challenges are likely to change across early development [14]. In addition, prior studies have not assessed variables that are theoretically and empirically linked to the psychological health of caregivers to children with developmental disabilities, such as parenting stress and coping strategies. The role of key family resources, such as food, shelter, financial resources, transportation, health care, and child care, as well as instrumental resources such as sufficient time to be with family, time for self, and emotional support, is also lacking in the literature. This knowledge is paramount in order to (1) identify caregivers and children at risk for poor functioning/developmental outcomes, (2) clarify areas of needed support, and (3) inform the development of interventions aligned with child needs and the family's needs and wishes.

Current study

The purpose of this project was to obtain information to inform the development of an ecologically valid and responsive support program to enhance the ability of family caregivers to promote the optimal development of their young children with CZS. Two specific aims were addressed. The first aim was to assess levels of anxiety and depression in caregivers of toddlers with confirmed CZS using well-validated, norm-referenced diagnostic measures. We hypothesized that the majority of caregivers surveyed would report moderate levels of anxiety and depression, with a small subgroup endorsing symptoms in the severe range.

The second aim was to identify child and family influences on levels of anxiety and depression in this Brazilian population of caregivers. Selection of constructs was informed by multidimensional conceptual models of caregiving process and caregiver well-being for parents of children with chronic illness and/or disabilities [32,33]. In these frameworks, background/contextual factors (e.g., socioeconomic status, family structure) and child characteristics (e.g., disability parameters) are specified as important but distal influences on caregiver well-being with psychosocial factors exerting a more proximal influence (e.g., stress, family coping, social support). Given evidence of conditional and indirect effects of psychosocial factors in the prediction of caregiver well-being [34], both main effects and interaction effects were of interest. We expected that higher anxiety and depression scores would be associated with having a younger child, having a child who is more dependent/has poorer health, having more young children in the home, lower family resources, lower family coping strategy use, and higher parenting stress. We also expected that both family resources and coping strategy use would interact with parenting stress in the prediction of anxiety and depression. Specifically, we anticipated that parenting stress would predict anxiety and depression at low but not high levels of family resources and family coping strategy use.

Materials and methods

Participants and setting

Participants were 50 caregivers of young children with CZS who were receiving medical care at the Instituto de Medicina Integral Professor Fernando Figueira, an institution accredited by the Ministry of Health of Brazil. This hospital is a located in Recife, the capital of Pernambuco, the epicenter of Brazil's Zika virus outbreak. Instituto de Medicina Integral Professor Fernando Figueira is part of the SUS network services (i.e., public system of health care) and is the only Clinical Research Center in Pernambuco to be accredited by the Ministry of Science and Technology. The institution is also certified by the Ministries of Health and Education as a Teaching Hospital and was the first hospital in Brazil to receive the title "Friend of the Children Hospital" from the World Health Organization/UNICEF/Brazilian Ministry of Health. Eligibility criteria specified that participants must be the primary caregiver to a child between the ages of birth to three years who has been diagnosed with CZS and is receiving weekly rehabilitation services at the center. The study was open to all caregivers regardless of race/ethnicity, gender, and age.

Procedure

Participants were recruited on site at the Instituto de Medicina Integral Professor Fernando Figueira hospital during their child's weekly therapy appointments. Trained, graduate-student research assistants approached caregivers to introduce the study and determine eligibility and interest. If a participant was eligible and expressed interest in participating, the research assistant obtained written informed consent. After obtaining consent, participants were asked whether they wished to complete the study during that visit, or if they preferred to schedule a study visit to occur during their child's therapy appointment the next week. Research assistants met with each participant individually to administer the study questionnaires in a private space at the hospital clinic. Visits took approximately 60–90 min. Participants' responses to the questionnaires were recorded electronically using iPads with Qualtrics to facilitate data management, ensure participants' confidentiality, and reduce data entry errors. Per hospital requirements, no incentives were provided to individual participants for their study participation. In lieu of direct participant incentives, a monetary donation was made to the hospital to purchase toys for the clinic spaces where children with CZS and their families received treatment and/or consultation. Data collection occurred between January 2018 and April 2018. This study is part of a larger project that was reviewed and approved by the Institutional Review Board at the University of Nebraska-Lincoln in the USA and the ethics committee of the Instituto de Medicina Integral Professor Fernando Figueira hospital in Brazil.

Measures

Beck Anxiety Inventory

Symptoms of anxiety were measured using the Brazilian Portuguese version of the Beck Anxiety Inventory [35–37]. Caregivers rated how much they have been bothered by 21 symptoms over the past week using a four-point scale ranging from 0 to 3. Items were summed to obtain a total score ranging from 0 to 63. Sum scores were interpreted as follows: 0–7 = minimal anxiety, 8–15 = mild anxiety, 16–25 = moderate anxiety, 26–63 = severe anxiety. This version of the Beck Anxiety Inventory has high internal consistency and item-total correlations

from 0.30 to 0.71 (median = 0.60) and has demonstrated high test–retest reliability and convergent validity with other scales [35]. Cronbach's alpha in the current sample was 0.90.

Beck Depression Inventory-II

Caregiver depressive symptoms were assessed using the Brazilian Portuguese version of the Beck Depression Inventory-II [38,39]. The Beck Depression Inventory-II is a 21-item inventory that measures characteristic attitudes and symptoms of depression. Respondents rate how they are bothered by each symptom using a 0–3 rating scale, yielding total scores ranging from 0 to 63. Suggested threshold for levels of severity is as follows: 0–13 = minimal/no depression, 14–19 = mild depression, 20–28 = moderate depression, and 29–63 = severe depression. This version of the Beck Depression Inventory-II has high internal consistency and factorial validity [38,40]. Cronbach's alpha in the current sample was 0.89.

Child dependence/health status

A composite proxy measure capturing the degree of children's dependency and health problems was created based on caregivers' responses to questions regarding their child's physical abilities and health status/needs. First, caregivers' overall rating of their child's health status was recoded into an indicator variable (0 = child's health is excellent, very good, or good; 1 = child's health is fair or poor). Next, caregiver responses to five items assessing the child's motor development were recoded as follows: child is able to sit alone (1 = no; 0 = yes); child stands alone or with help (1 = no; 0 = yes); child walks with help (1 = no; 0 = yes); child walks independently (1 = no; 0 = yes); child is able to sit in the bath (1 = no; 0 = yes). Finally, a composite score was calculated using the six recoded variables along with the following four indicator variables: child has a condition or disability in addition those associated with CZS (0 = no; 1 = yes); child has an illness or condition that requires continuous medical care (0 = no; 1 = yes); child's care requires special foods or equipment (0 = no; 1 = yes); and child has a feeding tube (0 = no; 1 = yes). The resulting composite score had a possible range from 0 to 10, with higher scores indicative of greater child dependence and poorer health.

Parenting Stress Index, Fourth Edition-Short Form

Caregivers responded to 36 interview statements on the Parenting Stress Index, Fourth Edition-Short Form using a five-point scale (1 = "I strongly agree" to 5 = "I strongly disagree") [41]. In addition to a Total Stress score, the Parenting Stress Index, Fourth Edition-Short Form allows for computation of three sub-scales and are computed: *Parental Distress* subscale measures distress the parent is feeling as it relates to parenting, including distress associated with diminished feelings of parenting competence, restrictions associated with parenting a small child, lack of social support, and depression. The *Parent–Child Dysfunctional Interaction* subscale measures how well the child meets the parent's expectations. The *Difficult Child* subscale assesses behavioral characteristics of the child and whether they are seen as easy or difficult to manage. The Parenting Stress Index, Fourth Edition-Short Form provides T scores and percentile scores as normative metrics. The normal range for scores in within the 16th and 84th percentiles. Scores in the 85th and 89th percentile are considered high, and scores above the 90th percentile are considered clinically significant. The psychometric properties of this measure have been established in a sample of mothers of infants [42]. The present study utilized the European Portuguese version of the Parenting Stress Index, Fourth Edition-Short Form, available

Table 1. Descriptive statistics for the study measures ($N = 50$).

Variable	M	SD	Observed range	Possible range	Kurtosis	Skew
Anxiety	4.8	5.1	0–20	0–63	−1.90	1.50
Depression	13.1	9.9	1–44	0–63	−0.70	1.00
Child dependence/health problems	6.0	2.1	1–9	0–10	0.08	−0.85
Family resources	79.0	22.0	31–124	30–150	−0.57	0.04
Caregiver coping strategy use	98.8	16.3	61–126	29–145	−0.55	−0.35
Parenting stress[a]	63.4	21.2	17–98	0–100	−0.55	−0.56

[a]Percentile scores reported.

from the publisher. As was done previously [43], some expressions were culturally adapted for use with our Brazilian Portuguese sample. Cronbach's alpha in the current sample for the Total Stress score was 0.89.

Family Crisis Oriented Personal Scales

The Family Crisis Oriented Personal Scales assesses problem solving, coping attitudes, and behavioral strategies used by families of children with disabilities in difficult or problematic situations [44]. Thirty items are divided into five different subscales: (1) acquiring social support from relatives, friends, neighbors, and extended family; (2) seeking spiritual support; (3) mobilizing the family to acquire and accept help from community resources and services; (4) reframing and redefining stressful situations in order to make them more manageable; and (5) passive appraisal, which is the family's ability to accept problematic issues while minimizing reactivity. Each item is measured on a five-point scale ranging from (1) strongly disagree to (5) strongly agree. A Total Caregiver Coping score is obtained by summing responses for each item, after reverse-scoring four items. A higher Total Caregiver Coping score indicates more use of both internal and external family coping strategies that aim to increase family resilience. The Family Crisis Oriented Personal Scales has good internal reliability ($\alpha = 0.87$). For the purpose of this study, this measure was subjected to linguistic and cultural adaptation following the three steps of forward translation, backward translation, comprehensibility testing [45]. Cronbach's alpha in the current sample for the Total Caregiver score was 0.84.

Family Resource Scale-Revised

The Family Resource Scale-Revised [46] was used to assess physical resources such as food, shelter, financial resources, transportation, health care, and child care, as well as instrumental resources such as sufficient time to be with family, time for self, and emotional support. Thirty items are measured on a five-point scale ranging from (1) not at all adequate to (5) almost always adequate. Responses are summed to calculate a Total Family Resources scale score, with higher values indicating more resources. The original Family Resource Scale has good reported internal reliability ($\alpha = 0.92$) [46]. For the purpose of this study, the Family Resource Scale-Revised was subjected to linguistic and cultural adaptation following the three steps of forward translation, backward translation, comprehensibility testing [45]. Cronbach's alpha in the current sample for the Total Family Resources scale was 0.90.

Statistical approach

Following established procedures [47], descriptive analyses (e.g., means, frequencies, proportions) were conducted to examine the distribution of all variables, screen for outliers, and ensure that primary model assumptions are met. To examine Aim 1, caregivers' total scores on the Beck Anxiety Inventory and Beck Depression Scale were categorized into severity levels for anxiety and depression following the established scoring conventions for each measure, and the percentage of caregivers falling into each category was determined. Hierarchical multiple linear regression models were estimated to identify the unique variance in anxiety and depression scores accounted for by family resources, coping strategy use, and parenting stress. Anxiety and depression served as the dependent variables in separate models. Family resource was entered in Step 1, coping strategy use was entered in Step 2, and parenting stress was entered in Step 3. Models predicting symptoms of anxiety and depression were estimated separately. Finally, moderation was tested in a multiple regression framework using the PROCESS v3 macro for SPSS (SPSS Inc., Chicago, IL) [48]. This macro uses Ordinary Least Squares regression to estimate direct and indirect effects in moderation models and provide simple slopes and regions of significance for probing interactions. The analysis was conducted using 5000 bootstrapped samples. Bootstrapping is an acceptable approach for use with samples of 20–80 [49]. Variables used to create interaction terms were mean-centered prior to model estimation. The significance level required to reject the null hypotheses was set at $p < 0.05$. All analyses were conducted using SPSS version 25 (SPSS Inc., Chicago, IL).

Results

Among the 50 caregivers who participated in the study, the majority (92%) were mothers (three identified as the child's grandmother, one was the child's father) and the mean age of participants was 31.1 years ($SD = 9.0$). The children were between seven and 37 months of age ($M = 25.9$, $SD = 6.2$) and 66% were female. Participants reported their race/ethnicity as follows: White (28%), Black (14%), Indigenous (4%), and Mixed race/ethnicity (54%). All of the participants reported a total family income between 1 and 3 minimum salaries, equivalent to approximately 300 USD per month. The majority (70%) had at least one other child within four years of age of the child with CZS living in the home.

Descriptive statistics for the study variables are presented in Tables 1 and 2. Regarding Aim 1, anxiety scores ranged from 0 to 20 ($M = 4.8$, $SD = 5.1$). The majority of participants (76%) endorsed minimal anxiety. The remainder reported mild anxiety (18%) or moderate anxiety (6%), with no participants endorsing symptoms in the severe range. Depression scores ranged from 1 to 44 ($M = 13.1$, $SD = 9.9$); over half of participants (60%) endorsed symptoms consistent with minimal/no depression and 20% endorsed mild depression. Another 12% endorsed moderate depression, and 8% endorsed symptoms at a level indicating the presence of severe depression.

The bivariate associations among study variables were examined to identity variables for inclusion in the regression models predicting caregiver anxiety and depression. Pearson's product moment correlations were used to examine the associations between continuous variables, and Spearman's rank order correlations were used to examined the associations between indicator variables. Results are summarized in Table 3. Child age, sex,

dependence/poor health, caregiver age, and the presence of other young children in the home were not significantly associated with anxiety or depression ($rs = -0.17$ to 0.23, ns). These variables were not included in subsequent multivariate models. A significant positive association was observed, however, between anxiety and depression ($r = 0.56$, $p < 0.001$). At closer look, higher anxiety scores were associated with lower family resources ($r = -0.36$, $p < 0.05$) and higher parenting stress ($r = 0.32$, $p < 0.05$). Higher depression scores were also associated with lower family resources ($r = -0.55$, $p < 0.001$) and higher parenting stress ($r = 0.65$, $p < 0.001$), but lower use of coping strategies ($r = -0.55$, $p < 0.001$).

Results of the hierarchical multiple regression analyses are summarized in Table 4. At Step 1, family resources contributed significantly to the prediction of anxiety, $F_{(1,48)} = 7.29$, $p < 0.05$, and accounted for 13% of the variance in this outcome. Introducing coping strategy use in Step 2 and parenting stress in Step 3 did not contribute significantly to the model (R^2 change $= 0.004$ and 0.027, respectively, ns). When family resources, coping strategies, and parenting stress were all included in the regression none of the variables significantly predicted anxiety.

A different pattern of findings emerged for depression. Results indicated that at Step 1, family resources contributed significantly to the prediction of depression, $F_{(1,48)} = 20.60$, $p < 0.001$, and accounted for 30% of the variance in depression. Introducing coping strategy use in Step 2 explained an additional 11% of the variance in depression and this change in R^2 was significant, $F_{(2,47)} = 8.65$, $p < 0.01$. Adding parenting stress in Step 3 explained an additional 13% of the variance in depression and this change in R^2 was significant, $F_{(3,46)} = 13.28$, $p < 0.01$. When family resources, coping strategies, and parenting stress were all included in the regression analysis only coping strategies and parenting stress significantly predicted depression. Together, the three independent variables accounted for 54% of the variance in caregiver depression scores, and the overall model was significant, $F_{(3,46)} = 18.10$, $p < 0.001$.

A moderation model using PROCESS was estimated to investigate whether depression was predicted by the interaction between parenting stress and coping strategies. Results indicated that the interaction term was significant ($B = -0.01$, $p < 0.05$, bias-corrected 95% bootstrapped CI $= -0.0127$ to -0.0014). To understand the nature of this interaction, we plotted conditional effects at low (16th percentile) and high (84th percentile) values of coping strategy use. As depicted in Figure 1, parenting stress was significantly and positively related to higher depression scores at low coping strategy use ($B = 0.36$, $p < 0.001$, bias-corrected 95% bootstrapped CI $= 0.228$–0.498), but not high coping strategy use ($B = 0.12$, ns, bias-corrected 95% bootstrapped CI $= -0.048$ to 0.285). Inclusion of the interaction term in the model resulted in a significant increase in variance accounted for by the predictors (F for change in $R^2 = 6.23$, $p < 0.05$). The overall model predicting depression was significant ($F_{(4,45)} = 20.26$, $p < 0.001$) and accounted for 64% of the variance in depression scores.

Discussion

The present study makes a unique contribution to the limited literature focusing on the psychological adaptation among caregivers to young children with CZS. The first aim of this study was to assess symptoms of anxiety and depression in these caregivers. Findings revealed that symptoms of depression were more prevalent among caregivers than symptoms of anxiety and affected nearly one-half of caregivers in our sample. Specifically, 12% of caregivers reported moderate depression symptoms and 8% severe depression symptoms, while another 20% of caregivers met criteria for mild depression. In general, this result is aligned with prior studies documenting poorer mental health outcomes among female caregivers to children with CZS [28–31]. Most recently, Kotzky et al. examined depression in caregivers of toddlers, and reported that 17.3% of caregivers to toddlers with Congenital Zika virus infection had scores on the Patient Health Questionnnaire-9 screening tool indicating moderately severe or severe depressive symptoms [31].

Our finding that moderate and severe symptoms of depression were more prominent in caregivers than moderate and severe symptoms of anxiety (20% versus 6%, respectively) is at odds with a prior finding that anxiety symptoms were common in mothers than symptoms of depression, with depression remaining low across the child's first year of life [28,29]. This finding is generally consistent with models suggesting that individuals' initial reactions to disability diagnosis/onset are characterized by shock, anxiety, and denial, later followed by the emergence of depression, internalized anger, and externalized hostility [50]. Indeed, heightened caregiver anxiety and stress in the acute stages of the child's illness or at the time of disability diagnosis is a normative response to an non-normative event in the family life cycle [51].

Table 2. Classification of caregivers based on severity of anxiety and depression symptoms ($N = 50$).

Variable	Minimal n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Anxiety[a]	38 (76)	9 (18)	3 (6)	0 (0)
Depression[b]	30 (60)	10 (20)	6 (12)	4 (8)

[a] 0–7 = minimal anxiety, 8–15 = mild anxiety, 16–25 = moderate anxiety, 26–63 = severe anxiety.
[b] 0–13 = minimal/no depression, 14–19 = mild depression, 20–28 = moderate depression, and 29–63 = severe depression.

Table 3. Bivariate associations among study variables ($N = 50$).

Variable	1	2	3	4	5	6	7	8	9
1. Child age	–								
2. Child sex	−0.11	–							
3. Child dependence/poor health	0.01	−0.13	–						
4. Caregiver age	0.23	−0.05	0.02	–					
5. Other young children in home	−0.06	−0.01	−0.27[†]	−0.26[†]	–				
6. Anxiety	0.04	0.11	−0.18	−0.07	0.00	–			
7. Depression	−0.08	−0.05	−0.11	−0.09	0.16	0.56***	–		
8. Family resources	0.08	0.32*	−0.17	0.06	−0.28*	−0.36*	−0.55***	–	
9. Caregiver coping	0.10	−0.02	0.21	−0.02	−0.29*	−0.23	−0.55***	0.48***	–
10. Parenting stress	−0.17	−0.09	−0.07	0.02	−0.31*	0.32*	0.65***	−0.47**	−0.44**

[†] $p < 0.10$.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

Table 4. Results of hierarchical regression analyses predicting caregivers' anxiety and depression scores ($N = 50$).

Variable	Model 1			Model 2			Model 3		
	B	SE B	β	B	SE B	β	B	SE B	β
Predicting anxiety									
Family resources	−0.08	0.03	−0.36*	−0.08	0.04	−0.33*	−0.06	0.04	−0.27
Caregiver coping				−0.02	0.05	−0.07	−0.01	0.05	−0.02
Parenting stress							0.05	0.04	0.19
R^2		0.13			0.14			0.16	
F for change in R^2		70.30**			0.21			10.48	
Predicting depression									
Family resources	−0.25	0.05	−0.55***	−0.16	0.06	−0.37**	−0.10	0.05	−0.23†
Caregiver coping				−0.23	0.08	−0.38**	−0.16	0.07	−0.26*
Parenting stress							0.20	0.06	0.43***
R^2		0.30			0.41			0.54	
F for change in R^2		20.60***			8.65**			13.28***	

†$p < 0.10$.
*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.

For most caregivers, the initial anxiety and stress reaction subsides, giving way to transitions to positive adaptation and resilience; however, a subset of caregivers to children with health and developmental conditions demonstrate ongoing or worsening psychological difficulties [52], including symptoms of depression [53]. Among parents of children with special health care needs, the risk for developing depression is associated with a loss of perceived control, elevated caregiving demands and burden, chronic stress and fatigue, diminished social support, reduced financial resources, and fatigue, guilt, and anticipatory grief [52–56]. These risk factors may become more prevalent for caregivers to children with CZS as their children age, making caregivers more vulnerable to depression as their children move from infancy into toddlerhood.

Alternatively, the contrasting findings regarding the relative prominence of depression versus anxiety symptoms in our sample versus prior studies may be an artifact of differences across studies in the measures used to assess anxiety and depression, as well as the differences in the timing of assessment (i.e., infancy versus toddlerhood). Regarding the latter, the higher anxiety scores observed in previous sample of mothers of infants with CZS may reflect normative anxiety reactions associated with the transition to parenthood, irrespective of the health status of the newborn. For example, longitudinal evidence suggests a trajectory of anxiety symptoms such that new parents experience mild anxiety in anticipation of their child's birth, which then decreases during the early postpartum months, eventually stabilizing at a low level toward the later postpartum period [57]. For parents who knew or suspected that their infant was affected by the Zika virus during pregnancy, this normal elevation in perinatal anxiety may have been compounded by uncertainty regarding their child's condition [58]. Ongoing longitudinal research describing the trajectories of psychosocial adaptation in caregivers of children with CZS is an important direction for future research.

Another objective of this study was to identify influences on caregivers' symptoms of anxiety and depression, drawing on a multifaceted theoretical model of caregiving and caregiver burden [33]. We hypothesized that higher anxiety and depression scores would be associated with having a younger child, having a child who is more dependent/has poorer health, having more young children in the home, lower family resources, lower coping strategy use, and higher parenting stress. This hypothesis was partially supported. Child characteristics, including child dependence/poor health, were not associated with either anxiety or depression. This result is at odds with a recent study comparing depression scores
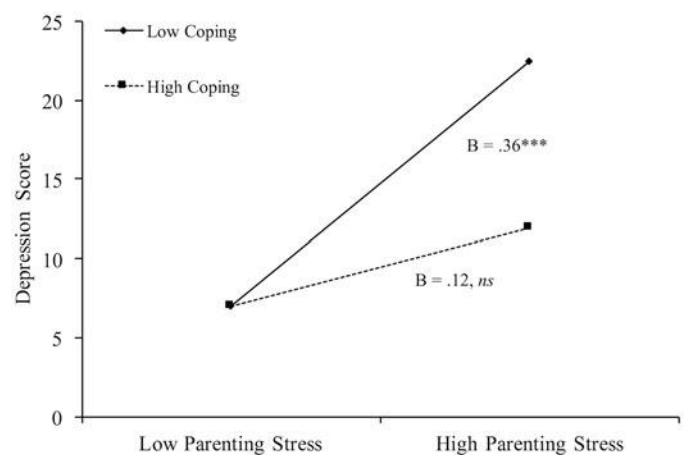

Figure 1. Caregiver depression is predicted by the interaction between parenting stress and use of caregiver coping strategies. Parenting stress is related to higher depression scores at low, but not high caregiver coping strategy use.

in caregivers to children with evidence of Congenital Zika virus infection [31]. Compared to caregivers of children without noted developmental delay, caregivers to children with developmental delay had higher depression scores. The extant research in broader samples of caregivers to children with disabilities also suggests that caregivers to children with more severe disabilities and/or poorer health are at elevated risk for psychological difficulties [59]. Thus, we believe that our results should be interpreted cautiously, as our proxy parent-report measure of children's functioning may not have accurately captured the extent of disabilities or indices of children's health status most strongly associated with anxiety and depression symptoms. Further research using direct assessment methods or clinical data from the child's medical chart is needed to better understand the links between children's heath/developmental status and their caregivers' psychological well-being.

Regarding family characteristics, we found that fewer family resources and more parenting stress were associated with symptoms of anxiety in bivariate analyses; however, these relationships were not evident in the multivariate model. For depression, bivariate analyses and multivariate analyses suggested that fewer family resources and coping strategy use, and more parenting stress were associated with higher depression scores. Together, these influences accounted for over half (54%) of the variance in caregiver depression scores. These findings are consistent with research testing prominent theories of caregiving processes and

caregiver adaptation for children with disabilities [33] and chronic health conditions [60], as well as empirical evidence from studies grounded in these conceptual frameworks. These findings point to the importance of focusing on family resources and coping strategy use trying to address depression in these caregivers. Health care providers should include assessment of coping strategies, parenting stress and family resources conjointly with evaluation of symptoms of depression and anxiety as part of routine CZS family evaluations.

A unique contribution of this study is that we explored the moderating effects of family characteristics in relation to depression scores. Exploration of conditional effects has not been conducted in any of the prior studies with caregivers to children with CZS, but can provide important information for the development of targeted intervention programs. Specifically, delineating the associations among factors that influence caregiver's psychological symptoms can help us to better identify caregivers most in need of intervention and tailor service provision to address their needs. To our knowledge, the only existing comprehensive support program for caregivers to children with CZS was developed based on general research on health promotion messaging, the determinants of poor health in caregivers, and common caregiving challenges for parents of children with disabilities [61]. Despite being informed by research, the benefits of this intervention may be limited if specific or unique challenges encountered by caregivers to children with CZS are not adequately addressed. In the present study, we expected that both family resources and coping strategy use would interact with parenting stress in the prediction of anxiety and depression. Specifically, we anticipated that parenting stress would predict anxiety and depression at low but not high levels of family resources and coping strategy use. Again, this hypothesis was only partially supported. Parenting stress was related to higher caregiver depression scores at low, but not high coping strategy use. This finding highlights the importance of assessing caregivers' coping strategies and their use in holistic evaluations of caregiver mental health risks in medical settings.

Overall, findings from this study highlight the need for interventions to address mental health, and specifically symptoms of depression, in caregivers of children with CZS who reside in low-income homes. The adverse effects of maternal depression on children's health and development during early childhood have been well-documented. In recognition of family mental health as a key influence on the developmental trajectory of children, making mental health services more accessible to caregivers has recently been identified as a global priority for supportive services for children with developmental delays and disabilities [25]. A useful approach for caregivers in Brazil may be to more fully integrate caregiver mental health support services into existing early intervention programs for children with CZS. In both theory and practice, early intervention is inherently family-centered as assessment and intervention services are undertaken with an understanding that child outcomes are strongly influenced by family needs, functioning, and strengths [62]. It may be particularly beneficial for professionals to increase their knowledge of particular family coping strategies that are malleable to change to increase a caregiver's psychological resilience in caring for a child with CZS. Moreover, it may be advantageous to examine ways to increase family resources and to examine depressive symptoms of women during pregnancy, as receiving a clinical diagnosis of Zika virus exposure significantly increases the likelihood of experiencing severe postpartum depressive symptoms immediately after the birth of the baby [63].

Strengths of this work include our use of well-established assessment measures, our focus on anxiety and depression in caregivers to toddler-aged children with confirmed diagnoses of CZS, and our exploration of caregiver and family contextual factors that have not been examined in prior research with CZS caregivers. Despite these strengths, several limitations of the study should be noted. Our sample of caregivers may not be representative of all caregivers to children with CZS. Our sample was entirely comprised of caregivers who are low-income and who were recruited from one hospital clinic. The extent to which our findings would generalize to more socio-economically diverse caregivers, or those who were not receiving intervention services at this hospital, is unknown. Moreover, with the exception of one father, all participants were female caregivers (i.e., mothers or grandmothers). Future studies enrolling both male and female caregivers as well as more representative samples are needed.

This was a cross-sectional study. As such, our results shed light on caregivers' symptoms of anxiety and depression, as well as their family resources, coping, and parenting stress, during a specific moment in time. Longitudinal studies that follow caregivers over time with repeated assessment of these factors would help to characterize changes over time and allow for inferences of causality to be examined. Another methodological limitation is that we did not have a comparison group of caregivers to healthy, typically developing children. Consequently, the precise impact of caring for a child with CZS on caregivers' mental health versus caring for a typically developing child, a child with another type of health condition, or other complex family life scenarios, cannot be determined. Future studies that include control group(s) can also consider other unique characteristics of the Zika virus outbreak that may help to understand any group differences in symptoms of psychological distress, such as media coverage or community awareness. The measures of family resources and coping strategy use were translated and culturally adapted for use in the present study. There is a need to evaluate the factor structure and psychometric properties of these measures with the Brazilian Portuguese speaking population to ensure their reliability and validity. All measures were obtained via caregiver self-report, which is subject to social desirability bias and recall bias. Finally, a limitation is that a standard measure of child functioning may have provided a more accurate assessment of child dependence/health status than our proxy composite measure. It is recommended that future studies use established measures, such as the Ten Questions Questionnaire [64].

In summary, despite the identified limitations, this study adds to the scant literature documenting the presence of mental health concerns in caregivers to children with CZS. This is the first study to explore the role of relevant family stress and resilience promoting factors (i.e., parenting stress, family resources, and coping strategies) in relation to caregiver anxiety and depression. In doing so, we address a knowledge gap identified in previous research with this population [21,30,31]. The findings presented in this study can be used to inform ongoing parent psychological support intervention programs in Brazil as well as the development of new programs designed to support caregivers to children with CZS in Brazil and other countries that may experience a Zika virus outbreak in the future.

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