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Depression, psychosocial correlates, and psychosocial resources in individuals with mast cell activation syndrome

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Abstract

Individuals with Mast Cell Activation Syndrome (MCAS), a rare chronic disease, experience unpredictable physical symptoms and diagnostic challenges resulting in poor emotional states. The prevalence and correlates of depressive symptoms were examined among 125 participants who completed the CES-D and relevant instruments. The majority reported a clinically-significant level of depression which was especially common among younger participants and those who reported greater loneliness or more disease-specific stressors. Greater magnitude of depressive symptoms was associated with greater illness intrusiveness, less social support, and lower optimism. Results highlight the value of interventions targeting loneliness and stressors unique to this population.

Keywords

depression; loneliness; mast cell activation syndrome; rare chronic illness; social support

> "The most stressful aspect of having this illness is, as it has always been, my lack of ability to participate in the tasks of daily life that healthy people can."
>
> -Study Participant

Introduction

Mast Cell Activation Syndrome (MCAS) is a rare chronic disease involving a severe systemic reaction to mast cell mediators (Valent and Akin, 2019), affecting fewer than 200,000 people worldwide at any one time. The physical symptoms associated with MCAS range in type, severity, location, duration, frequency, predictability, and controllability both within affected individuals over time and across individuals (Akin, 2014; Akin et al., 2010; Theoharides et al., 2015; Valent et al., 2012). Physical symptoms are a result of acute mast cell mediator release as is the case in anaphylaxis, or of chronic mast cell mediator release. These symptoms include fatigue, headache, angioedema, flushing, rash/hives, diarrhea,

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Supplemental material

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uterine cramps or bleeding, shortness of breath, blood pressure instability, acid reflux, muscle and bone pain, syncope, brain fog, and flushing (Theoharides et al., 2015; Valent, 2013; Valent et al., 2012).

Chronic illnesses that are rare, such as MCAS, typically impose a variety of hardships: they are unremitting, require ongoing medical attention, and are chronically disabling, among other burdens (Litterman et al., 2014; Wästfelt et al., 2006). Although there is considerable psychosocial research on common chronic illnesses such as rheumatoid arthritis and multiple sclerosis, rare diseases such as MCAS have historically received little attention from psychological science (Heemstra et al., 2009; Litterman et al., 2014; Wästfelt et al., 2006). In fact, to the best of our knowledge, no psychological studies have been conducted focusing exclusively on individuals with MCAS. However, nine studies have been conducted with individuals who have mastocytosis, a related but distinct type of mast cell disorder with similar symptomatology (Boddaert et al., 2017; Georgin-Lavialle et al., 2014, 2016; Hermine et al., 2008; Moura et al., 2011, 2012; Rogers et al., 1986; Siebenhaar et al., 2016; Vermeiren et al., 2020). In these studies, rates of depression are reported to be as high as 40%–70% (Georgin-Lavialle et al., 2014; Hermine et al., 2008; Moura et al., 2011, 2012; Rogers et al., 1986). Three studies have been conducted with individuals who have a variety of mast cell disorders including MCAS (Jennings et al., 2014, 2018; Nicoloro-SantaBarbara et al., 2017). In these studies, among individuals with any mast cell disorder, depression (Jennings et al., 2014; Nicoloro-SantaBarbara et al., 2017) was common as was poor quality of life (Jennings et al., 2014, 2018). Furthermore, higher physical symptom burden and poorer quality of life were associated with higher levels of depression (Nicoloro-SantaBarbara et al., 2017); poor quality of life was associated with the unpredictable nature of symptoms (Jennings et al., 2018).

Although there are accepted criteria for diagnosis of MCAS (Theoharides et al., 2015; Valent et al., 2012), limited physician knowledge and the non-specificity of symptoms often hamper and prolong accurate diagnosis (Hamilton et al., 2011; Jennings et al., 2014). As a result, people suspected to have MCAS may endure multiple referrals and recurrent hospital admissions, often with unnecessary testing and invasive procedures (Valent et al., 2012). For example, in order to meet the diagnostic criterion requiring evidence of mast cell activity, one must obtain a serum tryptase level laboratory test within 1–2 hours of a symptom flare-up (Valent et al., 2012), which is challenging for many people and providers to arrange (Cardet et al., 2013; Molderings et al., 2011). Fulfilling the diagnostic criterion that requires response to medication can also be difficult as people suspected to have MCAS frequently try several medications before symptoms resolve (Valent, 2013). Picard et al. (2013) found that approximately half of patients experience little or no benefit of medication. For such reasons, a large portion of people suspected to have MCAS do not ultimately meet the diagnostic criteria for MCAS although they have already had extensive medical evaluations (Valent et al., 2018). This is likely quite distressing for patients who may have been told initially by an allergist or other physician that they have MCAS and then learn from a specialist that they don’t meet the diagnostic criteria.

Yet even patients who receive a confirmatory diagnosis are likely to experience other stressors. Because MCAS is not well-recognized by the public, people with this disorder

may be stigmatized or viewed as malingerers by family, friends, co-workers, and other members of their social network as occurs even for more common and well-recognized disorders (e.g. Åsbring and Närvänen, 2002; Jacoby and Austin, 2007). In addition, because of its rarity, someone with MCAS is unlikely to meet another person with the disorder, which may result in loneliness and a sense of isolation. Apart from these stressors associated with having a rare disease, people with MCAS also experience the difficulties that are common to any chronic illness, including often-unpredictable and uncontrollable symptoms that disrupt activities of daily living and may interfere with employment and interpersonal relationships (Dehnavi et al., 2015).

Given its complex clinical presentation, including potentially life-threatening anaphylactic reactions (Butterfield, 2006), complicated diagnostic criteria (Valent et al., 2012), limited physician familiarity leading to delay in diagnosis (Jennings et al., 2018), and no cure (Valent et al., 2012), and in conjunction with what is already known about chronic illness from existing research, we reasoned that depression would be common among individuals with MCAS. However, reliable estimates of the prevalence of depression in this population are largely nonexistent. Documenting levels, types, and contributors to depression in this population can facilitate the development of appropriate interventions and highlight pathways through which emotional states such as depression may exacerbate MCAS symptoms, as hypothesized by some researchers (Theoharides and Konstantinidou, 2007). There is considerable evidence in other populations that negative emotional states can influence physical health through a variety of pathways (e.g. Cohen et al., 2007; Graham-Engeland et al., 2018; Hawkley and Cacioppo, 2010; Kiecolt-Glaser et al., 2015; Martin-Subero et al., 2016; McEwen and Gianaros, 2010; Miller and Raison, 2016; Slavich and Irwin, 2014); a number of these are implicated in MCAS, including the immune, neuroendocrine, and central nervous systems. Depression can also influence health behaviors, self-care, and compliance with medical regimens that are relevant to MCAS (Bauer et al., 2012; DiMatteo, 2000).

Study purpose

One aim of this study was to assess the prevalence of depression in individuals diagnosed with MCAS. We predicted that the rate of clinically-defined depression would be at least as high as the two-thirds rate found in a prior study of people with a variety of mast cell disorders including MCAS (Nicoloro-SantaBarbara et al., 2017).

A second aim was to examine psychosocial factors likely to be associated with depression in this population. To do this, we focused both on the presence of clinically defined depression, and also with the degree of depressive symptomatology in recognition of the possibility that psychosocial conditions may contribute to depressive state even at sub-clinical levels. We examined two sets of factors, not previously examined in individuals with MCAS, likely to be associated with depression: adverse *psychosocial correlates* that have been shown previously to be associated with poorer emotional states in chronically ill individuals, namely stigma, loneliness, disease-specific stress, and illness intrusiveness (Cacioppo et al., 2006; Fisher et al., 2007; Goudsmit et al., 2009; Kane, 2007; Taft et al., 2013), and *psychosocial resources* that are likely to alleviate depression in individuals with MCAS,

including optimism, self-efficacy, and social support. These resources have been shown to predict better emotional states in other populations coping with chronic illness (see Marks, 2014; Stanton et al., 2007; see review by Carver et al., 2010).

Methods

Overview

The current study analyzes data from a larger study on individuals with a chronic disorder (Nicoloro-SantaBarbara, 2019); here we report on those with MCAS and only results for variables pertinent to our hypotheses about that group. For the larger study, English speaking adults 18 or older with any type of chronic illness were invited to complete an anonymous, 90 minute Internet-based survey about their "experience of having a chronic illness." The study was approved by the Institutional Review Board of Stony Brook University and carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). To recruit participants with various chronic disorders for the larger study, we advertised the study on numerous sites, including the website, Facebook page, and newsletter of The Mastocytosis Society, a non-profit organization for patients and families affected by mast cell disorders. The study was also advertised on the website of the National Organization for Rare Disorders (NORD), a non-profit advocacy organization. A total of 125 participants with MCAS responded.

Measures

Depression.—The Center for Epidemiologic Studies Depression Scale (Radloff, 1977; CES-D) is a reliable, well-validated 20-item self-report measure (e.g. "Feel everything you did was an effort") that assesses frequency of depressive symptoms within the past month from 0 (none of the time) to 3 (almost all the time). A score of 16 or greater indicates a clinically-defined level of depression (Radloff, 1977) and was the threshhold used to identify depression among a prior study of individuals with mast cell disorders including MCAS (Nicoloro-SantaBarbara et al., 2017). The CES-D has excellent internal consistency as confirmed in this study (Cronbach's $\alpha = 0.91$). Analyses were conducted using a dichotomized variable, indicating whether a participant was above or below the clinically defined cut-off for depression, and a continuous score, representing variability in depressive symptoms in individuals irrespective of whether they are above the clinical threshold.

Psychosocial correlates

Stigma.—Stigma, the process of believing negative public attitudes about oneself (Corrigan and Penn, 1999; Corrigan et al., 2006), was assessed using the 8-item Stigma Scale for Chronic Illnesses-Short Form (SSCI-8; Molina et al., 2013). The SSCI-8 assesses the frequency with which an individual experiences enacted and internalized stigma (e.g. "Because of my illness, some people seem uncomfortable with me") rated on a 5-point scale from 1 (never) to 5 (always). Cronbach's α was 0.89.

Loneliness.—The Three-Item Loneliness Scale (Hughes et al., 2004) is a validated, abbreviated version of the 20-item Revised UCLA Loneliness Scale (Russell et al., 1980). It

includes three items (e.g. “How often do you feel isolated from others”), rated on a 3-point scale from 1 (hardly ever) to 3 (often). Cronbach’s α was 0.76.

Disease-specific stressors.—The 24-item Disease-Specific Stressors Questionnaire is a modified version of the Mast Cell Disorder Questionnaire (MCDQ; Nicoloro-SantaBarbara et al., 2017) which was expanded to include additional items relevant to unique stressors of chronic illness (e.g. “I’m tired of having to keep proving to people that I have a real illness”). Responses are on a 5-point scale from 0 (Never) to 4 (Very often). Cronbach’s α was 0.79.

Illness intrusiveness.—Illness intrusiveness, defined as the extent to which an illness or its related treatments affect an individual’s functioning (Devins, 1994), was assessed using the Adapted Illness Intrusiveness Rating Scale (AIIRS; Devins, 1994; Devins et al., 1984). The rating scale includes a stem (“How much does your illness and/or its treatment interfere with…”) and 13 items (e.g. “Your feeling of being healthy?”). Respondents indicate the degree of interference from 1 (not very much) to 7 (very much) for each item. Cronbach’s α was 0.82.

Psychosocial resources

Optimism.—Trait optimism, or possessing a generally positive outlook on life circumstances (Scheier and Carver, 1987), was assessed using the widely-used Revised Life Orientation Test (LOT-R; Scheier et al., 1994) which includes 10 items (e.g. “In uncertain times, I usually expect the best”), rated on a 6-point scale from 0 (“I disagree a lot”) to 5 (“I agree a lot”). Cronbach’s α was 0.82.

Self-efficacy.—Confidence in one’s ability to control symptoms and to secure a desired outcome (Felton and Revenson, 1984) was assessed using the Stanford Self-Efficacy for Managing Chronic Disease instrument (SECD; Lorig et al., 2001). The SECD includes six items (e.g. “How confident are you that you can keep the physical discomfort or pain of your disease from interfering with the things you want to do”), rated on a 10-point scale from 1 (not at all confident) to 10 (totally confident). Cronbach’s α was 0.80.

Social support.—The 20-item Medical Outcomes Study-Social Support (MOS-SS; Sherbourne and Stewart, 1991), a psychometrically sound instrument that was developed for patients with chronic conditions, was used to measure perceived functional social support. Respondents indicate “how often someone is available” if each type of support were needed (e.g. “to listen to you,” “to take you to the doctor”) on a 4 point scale from 1 (none of the time) to 5 (all of the time) (Sherbourne and Stewart, 1991). Cronbach’s α was 0.96.

Results

Data preparation

To prepare the data for all subsequent analyses, summary statistics including means, standard deviations, and frequencies were examined to ensure that all values were within range and showed sufficient variation between participants (see bottom of Table 2). Each

variable was examined for missing values. Roughly 56.6% of items for Disease-Specific Stressors and Self-Efficacy were missing, which was likely attributable to the length of the survey as both questionnaires were at the end. Therefore, pairwise deletion was used in some analyses to maximize power given the novelty and importance of the present investigation and a desire to retain all participant data. The pattern of findings was generally the same when these analyses were repeated using listwise deletion. Listwise deletion was used in all binary logistic regression analyses, as required (IBM Corp, 2017).

Sample description.—As shown in Table 1, a majority of the 125 participants were White, female, partnered, college-educated, unemployed, with an annual household income of $60,000 or less.

Average stigma (M = 23.16; SD = 6.66) corresponded to a score of “always” on the SSCI-8 (Molina et al., 2013), average illness intrusiveness (M = 78.16; SD = 14.68) corresponded to a score of “very much” on the AIIRS (Devins et al., 1984), and average loneliness (M = 7.01; SD = 1.72) corresponded to a score of “often” on the UCLA Loneliness Scale (Hughes et al., 2004).

Regarding disease-specific stressors, on average, the stressors endorsed as most frequent pertained to “feeling different from others” (M = 3.22, SD = 0.91), “lack of treatment or no treatment available for their illness” (M = 3.03, SD = 0.96), “feeling isolated” (M = 3.01, SD = 0.94), “tired of having to keep proving to people their illness is real” (M = 2.93, SD = 1.09), and “defective because of their illness” (M = 2.67, SD = 1.29).

Average optimism (M = 17.89; SD = 5.04) corresponded to a score of “I agree a lot” on the LOT-R (Scheier et al., 1994). Average availability of functional social support (M = 64.53; SD = 18.02) corresponded to a score of “all of the time” on the MOS-SS, and average self-efficacy (M = 21.28; SD = 11.15) corresponded to a score of “totally confident” on the SECD (Thompson et al., 2017; see bottom of Table 2).

Clinical depression.—Almost three-quarters of the sample (70.4% of the 107 who completed the CES-D) were clinically depressed as defined by a CES-D score ⩾16. When using a more stringent cut-off score of 27, which has been suggested for use among those with a chronic illness (Geisser et al., 1997), more than half of the sample were clinically depressed (56.07%). The mean sample CES-D score was 27.74 (SD = 11.75), which is higher compared to individuals with arthritis or inflammatory bowel disease (Sirois and Wood, 2017). Clinically depressed participants were younger (M = 38.97 years, SD = 10.68) than non-depressed participants (M = 47.68 years, SD = 18.04; $t(85) = -2.03$, $p < 0.02$). The prevalence of clinical depression did not differ by gender, income level, employment status, education, race, or marital status.

As shown in Table 3, univariate *t*-tests indicated that clinically depressed participants ($n = 88$) reported significantly more stigma, loneliness, illness intrusiveness, and disease-specific stressors than non-depressed study participants ($n = 19$). Depressed participants also reported significantly less optimism, self-efficacy, and social support.

Associations with clinical depression.—Binary logistic regression was used to determine the independent association of psychosocial correlates of chronic illness with clinical depression while controlling for age. This multivariate analysis indicated that clinical depression was more common among participants who reported greater loneliness (B = 3.48, SE = 1.46, Wald = 5.68, Exp(B) = 32.56, $p < 0.02$) and disease-specific stressors (B = 4.21, SE = 1.71, Wald = 6.05, Exp(B) = 67.59, $p < 0.01$). Depression was not independently associated with stigma (B = −1.19, SE = 0.86, Wald = 1.94, Exp(B) = 0.30, $p = 0.16$), illness intrusiveness (B = 0.62, SE = 0.62, Wald = 0.99, Exp(B) = 0.30, $p = 0.16$), or age (B = −0.03, SE = 0.04, Wald = 0.51, Exp (B) = 0.51, $p = 0.47$) in the multivariate analysis.

A second binary logistic regression analysis examined the independent association of psychosocial resources with clinical depression while controlling for age. This multivariate analysis indicated that clinical depression was significantly more common among participants who did not possess an optimistic disposition (B = −1.29, SE = 0.58, Wald = 4.97, Exp(B) = 0.28, $p = 0.03$). Social support (B = −0.90, SE = 0.48, Wald = 3.54, Exp(B) = 0.41, $p = 0.06$), self-efficacy (B = −0.22, SE = 0.26, Wald = 0.72, Exp(B) = 0.80, $p = 0.40$), and age (B = −0.03, SE = 0.32, Wald = 0.67, Exp(B) = 0.97, $p = 0.41$) were not uniquely associated with the presence of clinical depression.

The three significant predictors of clinical depression that emerged from these regression models (loneliness, disease-specific stressors, and optimism) were then examined simultaneously. This analysis revealed that clinical depression was uniquely more common among participants with greater loneliness (B = 2.90, SE = 1.20, Wald = 5.82, Exp(B) = 18.25, $p < 0.02$) and more disease-specific stressors (B = 3.36, SE = 1.44, Wald = 5.45, Exp(B) = 28.88, $p < 0.02$). Optimism was not uniquely associated with the presence of clinical depression after controlling for loneliness and disease-specific stressors (B = −0.37, SE = 0.62, Wald = 0.35, Exp(B) = 0.69, $p = 0.56$).

Associations with level of depressed mood.—Multiple linear regression with pairwise deletion was used to examine the independent association of psychosocial correlates with the continuous depression score, controlling for age. This analysis revealed that higher loneliness (B = 0.43, $p < 0.01$), disease-specific stressors (B = 0.29, $p < 0.03$), and illness intrusiveness (B = 0.13, $p < 0.01$) were independently associated with greater depressive symptomatology. Stigma (B = −0.06, $p = 0.45$) and age (B = −0.01, $p = 0.21$) were not uniquely associated with the magnitude of depressive symptoms. This model accounted for 53% of the variance in depressive symptomatology, $F(5,62) = 14.218$, $p < 0.00$. The model was re-tested using listwise deletion; the pattern of results was the same.

The second model of depressive symptomatology included psychosocial resources while controlling for age. Less social support (B = −0.19, $p < 0.01$) and lower optimism (B = −0.32, $p < 0.01$) were uniquely and significantly associated with depressive symptomatology. These variables accounted for 45% of the variance in depressive symptomatology, $F(4, 63) = 13.12$, $p < 0.01$. Using listwise deletion produced the same pattern of results.

When the significant psychosocial correlates and resource variables associated with depressive symptomatology were simultaneously examined, results revealed that participants who reported greater illness intrusiveness (B = 0.23, $p < 0.01$), lower optimism (B = −0.30, $p < 0.01$), or less social support (B = −0.21, $p < 0.01$) experienced more depressive symptoms. This model accounted for 61% of the variance in symptoms of depression, $F(3,72) = 38.09$, $p < 0.01$. When listwise deletion was used to test this model, loneliness was an additional significant predictor in the expected direction; this model predicted 61% of variability in the magnitude of depressive symptomatology

Discussion

Depression and psychosocial associations

To the best of our knowledge, this is the first scientific investigation of the psychological and emotional experience of a sample comprised exclusively of people diagnosed with MCAS. Clinical depression was common in this sample, corroborating the 64% prevalence observed in an earlier study of individuals with mast cell disorders including MCAS (Nicoloro-SantaBarbara et al., 2017). Almost three-quarters of individuals with MCAS in the current study reported clinically meaningful levels of depressive symptoms. Clearly, many individuals in this study are suffering emotionally. The prevalence of depression and loneliness is far higher than for the American population (Hughes et al., 2004; Substance Abuse and Mental Health Services Administration, 2014), and also higher than for people with other chronic illnesses including lupus and inflammatory bowel disease (Sirois and Wood, 2017). Findings from the other measures administered in this study also offer a more detailed portrait of the types and extent of emotional distress that people with MCAS experience. MCAS sufferers reported that their illness intrudes in their employment, their ability to manage a household, their physical recreation and hobbies, and their social activities. Individuals with MCAS in the current study reported higher illness intrusiveness compared to individuals with multiple sclerosis studied with the same instrument (Devins et al., 1984). The most frequently reported stressors associated with having MCAS were feeling different from others, the lack of treatments, feeling isolated, having to prove to others that their illness is real, and feeling defective because of their illness. A recent study of individuals with unspecified mast cell disorders reported similar intrusions (Jennings et al., 2018).

Participants who were most lonely were more than twice as likely to have depression scores above the clinically defined threshold. Additionally, those who experienced more disease-specific stressors, higher illness intrusiveness, or who were less optimistic or had less social support reported more symptoms of depression whether or not their symptoms exceeded the threshold to be considered clinically relevant. Taken together, these results indicate that a variety of psychosocial factors are closely and independently associated with depression among individuals with MCAS. These factors include the unique burdens of this particular illness, as well as adverse psychological states and lack of interpersonal and intrapersonal resources that have been shown to be common in people with chronic illness.

Interestingly, although individuals in the curent study reported high levels of stigma compared to people with multiple sclerosis (MS), epilepsy, or Parkinson’s disease (Molina

et al., 2013) and lower scores of self-efficacy than those with other chronic illnesses (Lorig et al., 2001), stigma and self-efficacy did not have unique associations with depressed mood in this study. This is likely attributable in part to the overlap of these constructs with other study variables. One might assume, for example, that stigma would be strongly associated with depressed mood in a population experiencing a rare disease such as MCAS with unpredictable and uncontrollable symptoms, and indeed, stigma was a significant bivariate correlate of depression. Yet stigma as measured in this study was also highly correlated with loneliness, illness intrusiveness, and disease-specific stressors, which exhibited independent associations with clinical depression or depressive symptoms. This pattern of findings suggests that the association of stigma with depressed mood in participants may be explained by factors that were captured in other study assessments. Such processes warrant confirmation and closer investigation in studies that can examine them longitudinally. Similarly, self-efficacy has been shown to be a potent protector against emotional distress in individuals with a variety of chronic illnesses including rheumatoid arthritis, MS, chronic fatigue syndrome, and myasthenia gravis (Barlow et al., 2002a; Barnwell and Kavanagh, 1997; Findley et al., 1998; Parada et al., 2014), but in the present study, the association of self-efficacy with depressed mood may have been obscured by the former variable's strong associations with other study variables. Therefore, our results should not be construed as suggesting that factors such as stigma and self-efficacy are not contributors to depression for individuals with MCAS, but that longitudinal, multivariate analyses are needed to tease apart what each factor independently and uniquely contributes.

Among all study variables, optimism, loneliness, and disease-specific stressors were the variables most frequently observed to be independent predictors in models of clinical depression and of depressive symptomatology, suggesting that these variables may be particularly important risk and resilience factors for individuals with MCAS. Feeling alone, for example, may be a particularly potent aspect of having a rare disease (von der Lippe et al., 2017), and hence, a risk factor for depression in people with MCAS. In fact, research has shown that loneliness is an independent and significant predictor of depression, disrupted sleep, dysregulated neuroendocrine and immune responses, and high blood pressure in the general population (Cacioppo et al., 2002, 2006; Steptoe et al., 2005) and of morbidity and mortality for those living with cancer and cardiovascular disease (Cacioppo et al., 2002). Endorsement of loneliness was high in this study. Although rare diseases in total affect a large number of individuals in the United States, there are very few affected individuals with each disorder including MCAS; thus, study participants may have never met another person with their disease. Loneliness is thought to influence emotion regulation processes in depression (Marroquin, 2011). For example, lonely individuals tend to engage in more maladaptive emotion regulation strategies which are strongly associated with depression compared to individuals who report feeling socially connected (Marroquin and Nolen-Hoeksema, 2015).

Notably, despite their loneliness, study participants were characteristically quite optimistic compared to individuals with diabetes or MS or even compared with healthy individuals (Scheier et al., 1994), although given that trait optimism (the variable measured in this study) tends to be quite stable, their tendency toward optimism may have preceded the onset of their disease and not reflect a situational or state response to it. Nevertheless, optimism

may be a resilience factor for people with MCAS, protecting them from depression by cultivating practices that promote adjustment to chronic illness including salutary health behaviors and adaptive ways of coping (Carver et al., 1993; Schou et al., 2005).

Finally, disease-specific stressors also accounted for a unique portion of variance in most of the models of depression and depressive symptomatology tested in this study. Individuals with MCAS endorsed a variety of stressful aspects of their disease, and reported that these occur quite frequently ("very often" on average). More than 55 % of participants selected the highest possible response to indicate the frequency of occurrence of stressors such as "lack of available treatments" or feeling "different from others." The consistent, independent association of scores on this instrument with depression variables highlights that such disease-related experiences and situations may have powerful impact on the emotional state of people with MCAS, regardless of their psychological vulnerability (e.g. loneliness) or resilience (e.g. optimism).

Limitations, strengths, and implications

Extrapolating from the findings of this study must be done cautiously because of its small size and its correlational design. In an effort to capture a robust psychological portrait of chronic illness and the novelty of data collection from individuals with a rare chronic illness, people were asked to complete a long questionnaire (i.e. approximately 90 minutes) which may have created participant burden and even discouraged some from participating. Participants may also be nonrepresentative because they were recruited from patient advocacy groups and postings on social media websites. The resulting sample was predominantly White, well educated, and socioeconomically advantaged, with access to the Internet. Nevertheless, the present study offers a strong foundation for in-depth, systematic investigation with more diverse samples to understand the psychological and emotional experience of all individuals with MCAS. Future studies using longitudinal repeated measures designs are imperative to elucidate the directions of association among depression and potential predictor variables or consequences. Excellent models exist of studies using time-based daily diary methods to enhance the accuracy of repeated mood and physical symptom self-reports (e.g. Bolger et al., 2003). This could be especially helpful for studies of MCAS to differentiate triggers from impacts based on their temporal association with episodic and chronic symptoms. Because of the inflammation and weakened immune system that are characteristic of this illness, it is thought that MCAS may be particularly reactive to emotional distress (Theoharides and Konstantinidou, 2007). Adding biomarkers associated with stress, emotions, and disease progression in future studies would therefore be highly informative.

Many of the people with MCAS who participated in this study are depressed, lonely, and feel poorly understood. Some of the stressors that they experience may be modifiable. Interventions that target loneliness have shown promise for individuals with other chronic illnesses (see review by Masi et al., 2011) and may be especially effective in preventing or alleviating clinical depression among people with MCAS given that loneliness was the factor most strongly associated with it. Specifically, randomized control cognitive behavioral therapy (CBT) trials that focus on challenging maladaptive social cognitions have been

shown to be the most effective in reducing loneliness (see Masi et al., 2011). Because of the rarity of MCAS, it may not be possible to reduce isolation through in-person interactions with other MCAS sufferers, but the Internet is a powerful resource that could be harnessed for this purpose to improve self-management skills and help people adapt better to their chronic conditions. Patient groups, even virtually, might be an invaluable resource for people with this uncommon and poorly understood disorder, offering a means to exchange support and information. We know from other chronic conditions that peer-led Internet-based forums can aid in psychological adjustment to chronic illness as well as reduce loneliness (Bessaha et al., 2020; Weinert et al., 2008). Additionally, family support groups and information campaigns to educate the public about MCAS and other rare diseases may help to alleviate misunderstanding and insensitivity. Evidence-based interventions at the individual, family, community, and broader levels are critical tools to reduce the emotional suffering that is prevalent among people with MCAS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Sample characteristics.

	M (SD)	*n*	%
Age	41.40 (12.86)		
Gender			
Female		122	97.60
Male		2	1.60
Other		1	0.80
Missing		0	0.00
		125	100.00
Marital status			
Married or living with partner		71	56.80
Not married		41	32.80
Missing		13	10.40
		125	100.00
Education level			
High school graduate		18	14.40
Associate's degree		19	15.20
Bachelor's degree		41	32.80
Master's degree		20	16.00
Doctorate/Professional degree (Ph.D., M.D., J.D.)		10	8.00
Other		3	2.40
Missing		14	11.20
		125	100.00
Racial/ethnic background			0
White		103	82.40
African American		1	0.80
Hispanic		4	3.20
Asian American		0	0.00
Native American		2	0.00
Missing		15	12.00
		125	100.00
Employment			
Employed		42	33.60
Unemployed		70	56.00
Missing		13	10.40
		125	100.00
Annual household income			
Under $15,000		20	16.00
$15,001–$45,000		28	22.40
$45,001–$60,000		10	8.00
$60,001–$75,000		7	5.60

	M (SD)	*n*	%
$75,001 or more		45	36.00
Missing		15	12.00
		125	100.00

Table 2.

Correlations among study variables and continuous depression.

	Depression	Stigma	Loneliness	Disease-specific stressors	Illness intrusiveness	Optimism	Self-efficacy	Social support
Depression	1	0.361**	0.580**	0.533**	0.531**	−0.578**	−0.379**	−0.405**
Stigma	–	1	0.463**	0.421**	0.369**	−0.249*	−0.200	−0.251**
Loneliness	–	–	1	0.354**	0.314**	−0.346**	−0.263**	−0.516**
Disease-specific stressors	–	–	–	1	0.470**	−0.564**	−0.502**	−0.173*
Illness intrusiveness	–	–	–	–	1	−0.225**	−0.114**	−0.008
Optimism	–	–	–	–	–	1	0.428**	0.157*
Self-efficacy	–	–	–	–	–	–	1	0.213*
Social support	–	–	–	–	–	–	–	1
M	27.73	23.16	7.01	45.86	78.16	17.89	21.28	64.53
SD	11.75	6.66	1.72	12.80	14.68	5.04	11.15	18.02
α	0.91	0.89	0.76	0.79	0.82	0.82	0.80	0.96

* $p < 0.05$.

** $p < 0.01$.

Table 3.

Comparison of clinically depressed and non-depressed participants.

	Depressed (CES-D ⩾ 16) (*n* = 102)		Non-depressed (CES-D < 16) (*n* = 23)		*n*	*t*
	M	**SD**	**M**	**SD**		
Stigma	24.08	6.34	18.50	6.57	76	2.96**
Loneliness	7.32	1.47	5.14	1.66	76	4.90***
Disease-specific stressors	48.26	10.46	34.00	10.05	68	4.17***
Illness intrusiveness	81.11	11.59	66.21	15.01	76	4.11***
Optimism	17.05	4.69	21.64	4.07	76	−3.38**
Self-efficacy	20.60	10.69	28.09	11.53	68	−2.10*
Social support[a]	62.35	17.82	77.21	12.88	104	−4.21**
Age[a]	38.97	10.68	47.68	18.04	106	−2.03*

[a]Levene's test for equality of variance indicated unequal variances between groups, so adjusted degrees of freedom were used.

*$p < 0.05$.

**$p < 0.01$.

***$p < 0.001$.