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Quality of life is impaired in myelin oligodendrocyte glycoprotein antibody associated disease

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Yana Said, Dimitrios C Ladakis, Julia M Lefelar, Jenny M Khazen, Jennifer Gould, Kathryn C Fitzgerald and Elias S Sotirchos

Abstract

Background: There is a paucity of studies examining quality of life (QoL) in people with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD).

Methods: A cross-sectional, online, self-administered survey was distributed. Data elements included demographic and clinical characteristics, and QoL in Neurological Disorders (Neuro-QoL) short form questionnaires. Neuro-QoL domain scores were compared to reference populations, yielding standardized T-scores. Symptom severity was categorized as mild, moderate, or severe, using standard Neuro-QoL cut points.

Results: A total of 259 participants completed the survey. Neuro-QoL domain impairment was present in a significant proportion of respondents (anxiety: 58.1%, depression: 30.7%, stigma 29.8%, cognition: 58.5%, social function: 57.7%). T-scores were significantly worse than the reference population for anxiety ($p<0.001$), stigma ($p=0.005$), cognitive function ($p<0.001$) and social interactions ($p<0.001$). There was no clear association between QoL domains and demographics, disease-modifying therapy class, or type of clinical presentation. A relapsing vs monophasic disease course was associated with worse anxiety, stigma, cognition, and social interactions ($p<0.05$).

Conclusion: People with MOGAD may exhibit impairment in multiple domains of QoL. Practicing clinicians should be aware of this burden in MOGAD. Further research is needed to better understand factors associated with QoL impairment in MOGAD.

Keywords: Myelin oligodendrocyte glycoprotein antibody associated disease, quality of life, anxiety, depression, social stigma, cognition, social interactions

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Introduction

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an autoimmune disease that impacts the central nervous system (CNS) and has been recognized as an entity that is distinct from other CNS inflammatory diseases, such as multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD).[1] Neurological deficits in MOGAD correlate to the anatomical site of involvement and can include visual dysfunction, limb weakness or paralysis, sensory loss and pain, bowel and bladder dysfunction, ataxia, seizures, and cognitive dysfunction, significantly impacting patients' activities of daily living.[1]

Prior studies have reported that MS and NMOSD have a substantial impact on patients' quality of life (QoL), however limited research on this topic has been conducted in MOGAD.[2–7] While recovery from attacks in MOGAD is generally better than in aquaporin-4 IgG seropositive NMOSD, and the disease may be monophasic in some patients, many people with MOGAD accrue permanent disability.[8]

In this cross-sectional survey, we performed a large-scale investigation of self-reported quality of life outcomes in adult and pediatric patients with MOGAD, examining the prevalence of anxiety, depression, stigma, cognitive function and their

Correspondence to:
Elias S. Sotirchos,
Department of Neurology, Johns Hopkins Hospital, 600 N. Wolfe St, Pathology 627, Baltimore, MD 21287, USA.
ess@jhmi.edu

Yana Said, Dimitrios C Ladakis,
Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Julia M Lefelar, Jenny M Khazen, Jennifer Gould,
The MOG Project, Olney, MD, USA

Kathryn C Fitzgerald, Elias S Sotirchos,
Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

ability to participate in social roles and activities. Additionally, we assessed patient satisfaction levels with their initial healthcare encounters and their current medical providers.

Methods

Standard protocol approvals and ethical considerations

The study protocol was reviewed by the Johns Hopkins University Institutional Review Board, and it was deemed to be an exempt study, as the survey was anonymous.

Study population and patient recruitment

The self-administered electronic survey was developed using RedCap and was distributed by The MOG Project (https://mogproject.org/ - an international advocacy group for MOGAD patients) through their online social media platforms and mailing list. The survey gave the option for caregivers to fill out the questions on behalf of patients. It also had auditory components to enable individuals who are blind or visually impaired to answer the questions with the help of a caregiver.

Survey components

The survey implemented the Quality of Life in Neurological Disorders (Neuro-QoL) tool, which is a collection of self-reported measures that assess the health-related quality of life of individuals, both adults and children, who are suffering from neurological disorders, such as MS, Parkinson's Disease, and epilepsy.[9–12] It evaluates 17 distinct domains related to quality of life, spanning physical, mental, and social health. For each domain, a set of questions has been developed for adult patients (≥18 years) and another set for pediatric patients (8- to 17-year-olds).[9] For this survey, the short form versions of the Neuro-QoL for the following domains were included: Anxiety, Depression, Stigma, Cognitive Functions, and Social Relations – Interaction with Peers (children) or Ability to Participate in Social Roles and Activities (adults). These domains were identified as key aspects of individuals' lives that may be affected by MOGAD after discussion with patients and patient advocates, and we focused on these specific domains (rather than including all Neuro-QoL domains) in order to optimize survey length and improve response rates. Patients less than 8 years of age were excluded from the Neuro-QoL related questions.

Each domain has 5–10 scaled questions, with a minimum raw score of 8 and a maximum raw score of 40.[9,11] A clinical reference sample from patients with various neurological conditions was used for stigma, whereas all other measures use a general U.S. reference population sample. Raw scores were compared to these populations, thus obtaining standardized T-scores, which have an average of 50 and a standard deviation (SD) of 10.[11] Higher scores indicate worse (undesirable) self-reported health for Anxiety, Depression and Stigma. In contrast, higher scores indicate better (desirable) self-reported health for Cognitive Function, Social Relations – Interaction with Peers and Ability to Participate in Social Roles and Activities. The severity of symptoms/impairment can be categorized based on the T-Score in comparison to the mean: having a score with 1.0 SD worse than the mean indicates mild symptoms, within 1.0–2.0 SD worse than the mean indicates moderate symptoms, and scores of 2.0 SD or more worse than the mean indicate severe symptoms.[9]

The survey also included questions related to participant demographics (sex, age, gender, race, residence) and clinical characteristics (initial symptoms, presentations, diagnostic lag, relapses, comorbidities, acute treatments and chronic medications, medical and psychiatric comorbidities). Additionally, Likert scaled questions related to patients' satisfaction with healthcare professionals were included.[13]

Statistical methods

We used linear regression models to examine associations of demographic and clinical characteristics with anxiety, depression, stigma, cognitive function, and social interactions. Each domain's T-score was treated as a continuous dependent variable. Analyses were performed with univariable models to assess the unadjusted association of each predictor with the dependent variable. Multivariable analyses were also performed to assess the independent association of each predictor (adjusted for the other variables in the model in order to account for potential confounding factors) with Neuro-QoL domains. We employed a single-sample t-test to compare the domain T-scores obtained from our survey respondents to the Neuro-QoL reference population T-scores. Spearman's rank correlation coefficient was used to assess the relationship between anxiety and depression Neuro-QoL T-scores with cognitive Neuro-QoL T-scores. Data visualization and analysis was conducted using R Studio Version 4.2.1 (https://www.r-project.org/). Statistical significance was defined as a p-value of less than 0.05.

Results

Patient demographics and characteristics

A total of 341 participants started the survey, 261 (77%) of whom submitted a complete record. Among the 261 participants, two indicated that they did not have a diagnosis of MOGAD. As a result, they were excluded from the analysis and our study focused on the records of the remaining 259 participants. Additionally, 11 completed surveys corresponded to patients less than 8 years of age; hence they were not eligible to complete the Neuro-QoL questionnaires.

Of the 259 participants, 50 (19%) were completed by caregivers on behalf of the participants, including 37 of 39 pediatric surveys. The detailed demographic and clinical characteristics of the study population are shown in Table 1. Of the respondents, 191 (74%) were females and 218 (84%) were White or Caucasian. The majority (71%) resided in North America, of which 93% were in the United States of America. A diverse representation of age groups was observed amongst the participants, with a significant mdxajority (85%) comprising individuals aged over 18 years. The most common initial clinical presentation was optic neuritis, comprising 41% of the respondents. Moreover, 60% had experienced a relapsing course (i.e., more than one attack), and 39% of respondents have experienced their last attack within 6 months prior to answering the survey. Long term maintenance therapy use for MOGAD relapse prevention was reported by 73% of respondents.

Quality of life domains

Anxiety. Out of the 220 adult participants, 125 (56.8%) exhibited mild, moderate, or severe anxiety (Table 2, Figure 1), as defined relative to the reference population. A diagnosis of Generalized Anxiety Disorder (GAD) was reported by 46 of these 125 adults (36.8%), whereas 37 (29.6%) of them reported taking medication prescribed for anxiety.

Of 28 pediatric patients aged between 8–17 years of age, 19 (67.9%) reported mild to severe anxiety symptoms, as compared to the reference pediatric population. Two of these 19 patients (10.5%) reported an established diagnosis of Generalized Anxiety Disorder, and one (5.3%) of them had been taking anti-anxiety medication.

Table 1. Patient demographics and clinical characteristics.

Characteristic, n (%)	N = 259
Respondent	
Caregiver	50 (19)
Patient	209 (81)
Sex assigned at birth, female	191 (74)
Age	
0–17 years old	39 (15)
18–34 years old	69 (27)
35–54 years old	94 (36)
55 + years old	57 (22)
Race, White or Caucasian	218 (84)
Current primary residence	
Africa	2 (0.8)
Asia	7 (2.7)
Europe	44 (17)
North America	185 (71)
Oceania	16 (6.2)
South America	5 (1.9)
Time between symptom onset and diagnosis, less than 6 months	167 (64)
Experienced more than one attack	155 (60)
Last attack, within the last 6 months	102 (39)
Type of attacks	
Acute Disseminated Encephalomyelitis and/or Encephalitis	59 (23)
Brainstem lesions	55 (21)
Optic Neuritis	178 (69)
Other/Not sure	49 (19)
Transverse Myelitis	85 (33)
Current treatment	
None	52 (20)
Biological agents[a]	31 (12)
Combination of treatments	68 (26)
Corticosteroids	31 (12)
Immunoglobulins	45 (17)
Oral immunosuppressants[b]	23 (8.9)
Other/Not sure	9 (3.5)
Comorbidities[c]	104 (40)
Psychiatric disorder[d]	113 (44)

[a]Biological agents include Tocilizumab and Rituximab.
[b]Oral immunosuppressants include Azathioprine and Mycophenolate mofetil.
[c]Comorbidities include diabetes, cancer any other autoimmune disease, and others.
[d]Psychiatric disorders include clinically diagnosed Depression, Post Traumatic Stress Disorder, Generalized Anxiety Disorder, Bipolar Disorder and others.

Table 2. Anxiety, depression, stigma, cognitive function, and social relations difficulty symptom levels in children and adults.

	Levels			
	Within normal limits	Mild symptoms[a]	Moderate symptoms[b]	Severe symptoms[c]
Anxiety				
Children *(N = 28)*	9 (32%)	8 (29%)	10 (36%)	1 (4%)
Adults *(N = 220)*	95 (43%)	38 (17%)	65 (30%)	22 (10%)
Total *(N = 248)*	104 (42%)	46 (19%)	75 (30%)	23 (9%)
Depression				
Children *(N = 28)*	19 (68%)	6 (21%)	2 (7%)	1 (4%)
Adults *(N = 220)*	153 (70%)	35 (16%)	26 (12%)	6 (2%)
Total *(N = 248)*	172 (69%)	41 (17%)	28 (11%)	7 (3%)
Stigma				
Children *(N = 28)*	20 (71%)	7 (25%)	1 (4%)	0 (0%)
Adults *(N = 220)*	154 (70%)	35 (16%)	28 (13%)	3 (1%)
Total *(N = 248)*	174 (70%)	42 (17%)	29 (12%)	3 (1%)
Cognitive function				
Children *(N = 28)*	16 (58%)	4 (14%)	4 (14%)	4 (14%)
Adults *(N = 220)*	87 (40%)	40 (18%)	72 (32%)	21 (10%)
Total *(N = 248)*	103 (41%)	44 (18%)	76 (31%)	25 (10%)
Social relations				
Children *(N = 28)*	15 (54%)	5 (18%)	7 (25%)	1 (4%)
Adults *(N = 220)*	90 (41%)	67 (30%)	57 (26%)	6 (2%)
Total *(N = 248)*	105 (42%)	72 (29%)	64 (26%)	7 (3%)

[a]Mild symptoms were attributed to those with scores 0.5–1.0 SD higher/worse than the mean for Anxiety, Depression and Stigma, and 0.5–1.0 SD lower/worse than the mean for Cognitive function, and Social relations.
[b]Moderate symptoms were attributed to those with scores 1.0–2.0 SD higher/worse than the mean for Anxiety, Depression and Stigma, and 1.0–2.0 SD lower/worse than the mean for Cognitive function, and Social relations.
[c]Severe symptoms were attributed to those with scores ≥ 2.0 SD higher/worse than the mean for Anxiety, Depression and Stigma, and ≤ 2.0 SD lower/worse than the mean for Cognitive function, and Social relations.

Overall, anxiety T-scores were significantly worse in patients with MOGAD compared to the general population (mean difference: 6.82 [95% CI: 5.61, 8.03]; $p < 0.001$). Higher anxiety T- scores were associated with a relapsing disease course (coefficient: 3.77 [95% CI: 0.61, 6.93]; $p = 0.02$), and with the use of psychiatric medications (coefficient: 4.78 [95% CI: 2.19, 7.37]; $p < 0.001$) **(**Supplemental Table 1).

Depression. At least mild depressive symptoms were reported by 67 (30.5%) adult participants (Table 2, Figure 1). Of these 67 individuals, 28 (41.8%) reported receiving a diagnosis of Major Depressive Disorder and 25 (37.3%) reported being treated with anti-depressant medication.

Of pediatric respondents, nine (32.1%) reported mild to severe depressive symptoms. A diagnosis of Major Depressive Disorder was reported by two (22.2%) of these symptomatic respondents, but none reported use of antidepressant medication.

T-scores among MOGAD patients were not significantly worse than the general population for depression (mean difference: −0.01 [95% CI: −1.23, 1,22]; $p = 0.99$). Higher depression T-scores were associated with the use of psychiatric medications (coefficient: 5.29 [95% CI: 2.61, 7.97]; $p < 0.001$; Supplemental Table 2).

Stigma. Mild to severe symptoms related to stigma were reported by 30.0% of adult participants and 28.6% of pediatric patients (Table 2, Figure 1), and stigma T-scores were significantly worse in MOGAD patients compared to the clinical reference population (mean difference: 1.39 [95% CI: 0.41, 2.36]; $p = 0.005$).

Worse stigma symptoms were associated with relapsing disease (coefficient: 4.54 [95% CI: 2.14, 6.94];

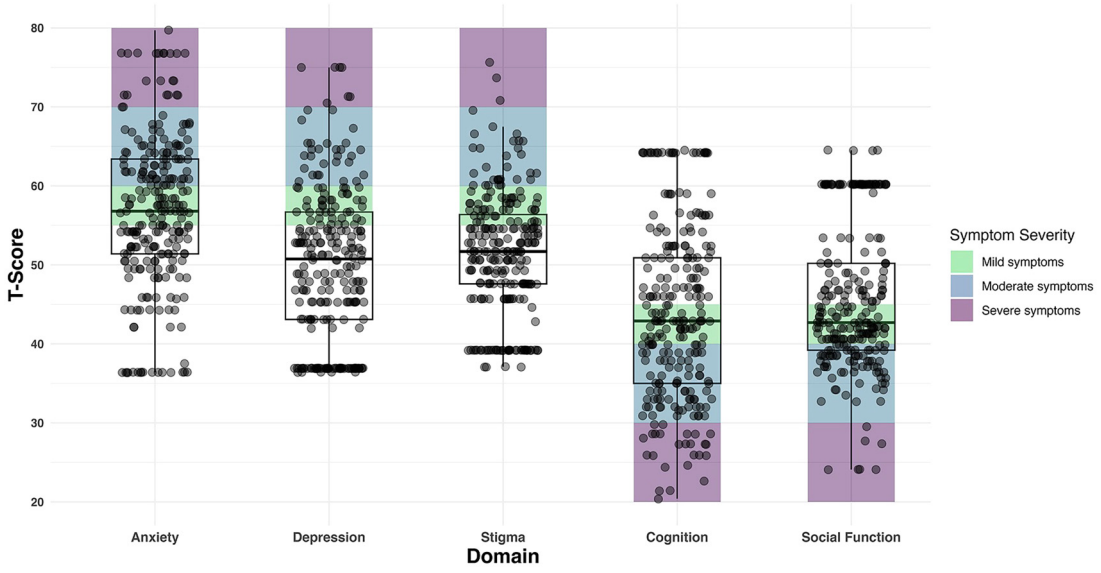

Figure 1. Neuro-QoL T-scores by domain for children and adult participants
For anxiety, depression and stigma domains: mild symptoms were attributed for those with scores 0.5–1.0 SD (or 5–10 points) higher/worse than the reference population's mean of 50. Moderate symptoms were attributed for those with scores 1.0–2.0 SD (or 10 to 20 points) higher/worse than the reference population's mean of 50. Severe symptoms were attributed for those with scores ≥ 2.0 SD (or ≥ 20 points) higher/worse than the reference population's mean of 50.
For Cognitive function and Social Relations domains: mild symptoms were attributed for those with scores 0.5–1.0 SD (or 5–10 points) lower/worse than the reference's population mean of 50. Moderate symptoms were attributed for those with scores 1.0–2.0 SD (or 10 to 20 points) lower/worse than the reference's population mean of 50. Severe symptoms were attributed for those with scores ≤ 2.0 SD (or ≤ 20 points) lower/worse than the reference population's mean of 50.

$p < 0.001$), presence of comorbidities (coefficient: 2.26 [95% CI: 0.24, 4.27]; $p = 0.03$) and use of psychiatric medication (coefficient: 2.92 [95% CI: 0.95, 4.88]; $p = 0.004$) (Supplemental Table 3).

Cognitive function. Mild to severe cognitive symptoms were reported by 60.5% of adult patients and 42.9% of pediatric patients (Table 2, Figure 1) and cognition T-scores were significantly worse among MOGAD patients compared to the general population (mean difference: −6.36 [95% CI: −7.74, −4.98]; $p < 0.001$).

Worse cognitive symptoms scores were associated with a relapsing disease course (coefficient: −8.17 [95% CI: −11.71, −4.64]; $p < 0.001$), presence of comorbidities (coefficient: −3.40 [95% CI: −6.37, −0.44]; $p = 0.03$), and use of psychiatric medication (coefficient: −4.05 [95% CI: −6.95, −1.15]; $p = 0.006$) (Supplemental Table 4).

Worse cognitive T-scores were associated with higher anxiety T-scores ($\rho = -0.48$, $p < 0.001$) and higher depression T-scores ($\rho = -0.48$, $p < 0.001$).

Ability to participate in social roles and activities / Social relations – Interaction with Peers. Mild to severe impairment in the ability to participate in social roles and activities was reported by 59.1% of adult participants, while difficulties in interacting with their peers were reported by 46.4% of pediatric patients (Table 2, Figure 1). T-scores were significantly worse than the general population for social interactions among MOGAD survey respondents (mean difference: −4.37 [95% CI: −5.52, −3.23]; $p < 0.001$).

Worse scores in these domains were associated with relapse within the last 6 months (coefficient: −3.18 [95% CI: −5.76, −0.60]; $p = 0.02$), relapsing disease course (coefficient: −4.06 [95% CI: −6.89, −1.23]; $p = 0.005$), presence of comorbidities (coefficient: −2.99 [95% CI: −5.37, −0.62]; $p = 0.01$) and use of psychiatric medications (coefficient: −3.95 [95% CI: −6.27, −1.63]; $p = 0.001$) (Supplemental Table 5).

Patient experience and satisfaction

A significant portion of participants (48%) agreed with the statement, "I felt dismissed or not taken seriously by healthcare professionals when I presented

with my initial symptoms (before my proper diagnosis with MOG-AD),” highlighting a concerning aspect of their healthcare journey (Figure 2). Conversely, 81% of respondents agreed with the following statement: “The healthcare professional who makes my treatment decisions takes my symptoms and medical concerns seriously” (Figure 2).

Discussion

In this cross-sectional survey, we found a high prevalence of impaired QoL in people with MOGAD, as compared to the reference Neuro-QoL population, with significant impairments observed in the domains of anxiety, stigma, cognitive dysfunction and social interactions. Exploratory analyses assessing association between QoL domains with clinical and demographic features identified a relapsing disease course as a factor associated with worse QoL, but no association was identified between QoL and other features.

There are few studies in the literature previously examining this topic, which applied different tools than our study to assess QoL in MOGAD.[3–5] Our study results largely align with their findings.[3–5] While most health-related QoL questionnaires are widely used and validated tools, they may not be sensitive or specific to capture the unique experiences and challenges faced by patients with neurological conditions, which drove us to use the Neuro-QoL. In our study, QoL among MOGAD patients was significantly worse than reference populations in most domains including anxiety, stigma, cognitive function, and social relations. While this is not an unexpected finding, MOGAD is generally considered to have a better clinical outcome and prognosis compared to MS and NMOSD, and it is important to highlight the physical and psychological challenges faced by MOGAD patients.

Notably, individuals experiencing a relapsing disease course manifested worse anxiety, stigma, cognitive function and social interaction QoL scores, a logical alignment given the potential psychological impact of these recurrent episodes. Concurrently, experiencing a relapse within the preceding 6 months was associated with a reduction in patients’ capacity to engage in social activities. This is not surprising, given their possible recuperation from deficits and ongoing rehabilitation, a process that might delay return to social activities. Notably, factors such as sex, treatment regimen, and presentation type exhibited no discernible impact on the QoL domain scores.

Those who were prescribed psychiatric medications exhibited a similar trend on all domains including depression, which is not unexpected and likely reflects the indication bias of receiving a prescription of such medications. Even though a subset of participants displaying symptoms of depression or anxiety were officially diagnosed and/or used psychiatric medication, this was not the case in the majority of participants with impairments in relevant QoL domains. This raises the possibility that these conditions may be underdiagnosed in people with MOGAD, and suggests that screening for such symptoms in clinical practice may be useful. The presence of additional comorbidities was associated with worse cognitive functioning, stigma perception, and social relations scores. This is likely attributed to the complexities and challenges of managing multiple health issues concurrently, which can affect patients’ overall well-being, influencing their cognitive

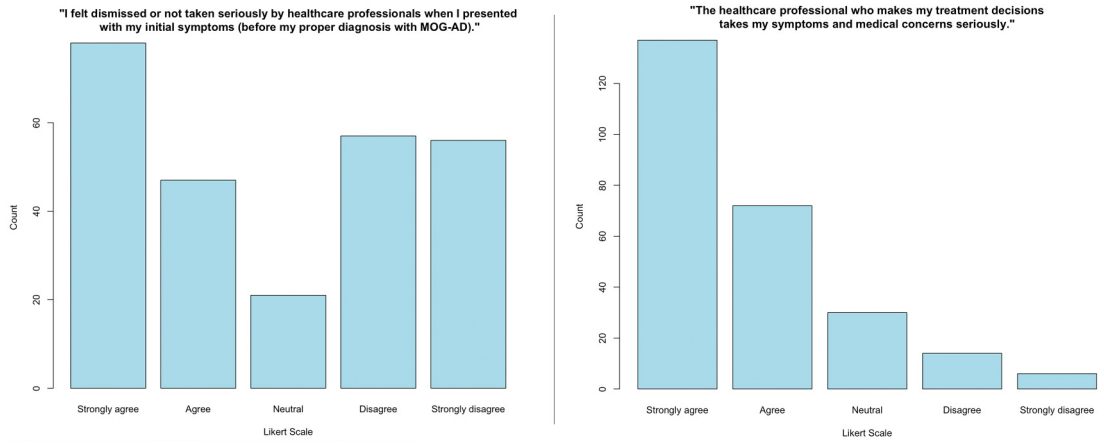

Figure 2. Patients satisfaction levels with healthcare professionals at initial encounter and at time of survey.

abilities, the way they are being perceived by their peers and the social interactions with them.

Our study underscores the significant burden of anxiety and cognitive impairment in MOGAD patients compared to the general population. Anxiety levels were particularly elevated in patients with a relapsing disease course, regardless of the timing of their last attack, indicating a pervasive psychological impact of MOGAD. The high prevalence of anxiety among pediatric patients is particularly concerning, raising questions about potential impacts on their developmental milestones. Additionally, there is a strong bidirectional relationship between anxiety/depression and cognitive dysfunction. Anxiety and depression can lead to cognitive impairment, while in return, cognitive deficits can intensify these psychological conditions.[14,15] This interplay underscores the need for comprehensive management strategies that address both psychological and cognitive health to improve the overall quality of life for MOGAD patients.

Additionally, our survey included questions regarding patient experience and satisfaction with their healthcare interactions. Our study revealed that approximately half of the participants endured feelings of dismissal and lack of seriousness during their initial attempts to seek medical care, shedding light on a disconcerting aspect of their experiences. Notably, the diagnostic process for MOGAD patients is often challenging, as the disease is relatively rare and recently recognized, and can present with symptoms similar to other CNS inflammatory disorders, with the potential for misdiagnosis and mistreatment.[16,17] The process could entail multiple consultations, unnecessary diagnostic tests, and conflicting opinions from healthcare professionals. However, most participants felt satisfied with their current medical care and believed that their healthcare providers are addressing their concerns properly.

It is important to acknowledge the limitations of our study, mainly stemming from the study design, as this was an anonymous online survey, which prevents us from examining characteristics associated with survey response or lack thereof. A potential selection bias emanates from the online survey administration, potentially constraining participation to those comfortable with digital platforms. Moreover, the recruitment of participants with a self-reported MOGAD diagnosis utilizing distribution of the survey via a patient advocacy organization network may have led to overrepresentation of individuals who are more likely to have a large impact of MOGAD on their lives leading to heightened engagement in advocacy, as well as some participants who might not actually have MOGAD, as misdiagnosis may occur, especially in patients with low-titer MOG-IgG seropositivity.[18] Furthermore, the potential for proxy bias arises, as caregivers' responses may not align with the lived experiences of MOGAD patients, introducing variation in question interpretation. A further bias is associated with the utilization of a quantitative research framework. While the survey yields valuable insights into patient experiences, it may not capture the full complexity and nuance of individual stories, which may be better explored through qualitative research methods. It is also important to note that there might have been other factors not included in our analyses that could have impacted patient's psychological state and quality of life, such as current physical disability, exercise, pain levels, and socioeconomic factors. Our findings are also limited by the demographic composition of our sample, which was predominantly North American and female. Future research should include a more geographically and gender-diverse population to enhance generalizability. Additionally, the cross-sectional design of this study does not capture the dynamic nature of the constructs being examined, as QoL can fluctuate over time. For instance, the timing of onset of anxiety and depression among patients who received a psychiatric diagnosis was not determined within this study, limiting our understanding of the relationship of these conditions to MOGAD.

In conclusion, our study highlights the impact of anxiety, depression, stigma on MOGAD patients' QoL, as well as the struggles they face participating in social activities and the cognitive challenges they must overcome. More comprehensive studies with clinic-administered surveys encompassing diverse patient-reported outcomes and QoL domains will be important to obtain a better understanding of the well-being of people with MOGAD, and allow a more detailed assessment of factors associated with impaired QoL.

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Data availability

The data used for this study are available from the corresponding author on reasonable request, with the proper data sharing agreements in place.

Declaration of conflicting interests

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ORCID iDs

Yana Said https://orcid.org/0009-0004-4350-1910
Dimitrios C Ladakis https://orcid.org/0000-0002-5764-2114
Kathryn C Fitzgerald https://orcid.org/0000-0003-3137-0322
Elias S Sotirchos https://orcid.org/0000-0002-8812-1637

Supplemental material

Supplemental material for this article is available online.

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