UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE

Ricardo Pereira Gonçalves

PERFIL DEMOGRÁFICO E PREVALÊNCIA DE ANSIEDADE NO PACIENTE COM ESCLEROSE MÚLTIPLA NO BRASIL DURANTE A PANDEMIA DE COVID-19

Porto Alegre
2021

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Dissertação submetida ao Programa de Pós-Graduação em Ciências da Saúde da Universidade Federal de Ciências da Saúde de Porto Alegre, como requisito para a obtenção do título de Mestre.

Orientador: Prof. Pedro Dal Lago

Porto Alegre-RS

2021

Catalogação na Publicação

Pereira Gonçalves, Ricardo
PERFIL DEMOGRÁFICO E PREVALÊNCIA DE ANSIEDADE NO PACIENTE COM ESCLEROSE MÚLTIPLA NO BRASIL DURANTE A PANDEMIA DE COVID-19 / Ricardo Pereira Gonçalves. -- 2021.
89 p. : il., tab. ; 30 cm.

Dissertação (mestrado) -- Universidade Federal de Ciências da Saúde de Porto Alegre, Programa de Pós-Graduação em Ciências da Saúde, 2021.

Orientador(a): Pedro Dal Lago.

1. esclerose múlipla. 2. ansiedade. 3. covid-19. 4. qualidade de vida. I. Título.

Sistema de Geração de Ficha Catalográfica da UFCSPA com os dados fornecidos pelo(a) autor(a).

FOLHA DE APROVAÇÃO

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C E R T I F I C A D O

Certificamos que **Ricardo Pereira Gonçalves** orientado pelo Prof. Pedro Dal Lago, apresentou a Dissertação de Mestrado intitulada "Perfil demográfico e prevalência de ansiedade no paciente com esclerose múltipla no Brasil durante a pandemia de Covid-19", no dia 15/10/2021, junto ao Programa de Pós-Graduação em Ciências da Saúde da Universidade Federal de Ciências da Saúde de Porto Alegre, sendo considerado **aprovado**. Após a homologação da Dissertação de Mestrado receberá o título de Mestre em Ciências da Saúde: Epidemiologia e Métodos Diagnósticos.

Porto Alegre, 15 de outubro de 2021.

Giovana Maria Roth Lopes
Secretária Executiva
PPG Ciências da Saúde - UFCSPA

AGRADECIMENTOS

Ao Programa de Pós–Graduação em Ciências da Saúde da Universidade Federal de Ciências da Saúde de Porto Alegre pela oportunidade da continuidade dos meus estudos;

Ao meu orientador Prof. Pedro Dal Lago pelos ensinamentos, pela paciência e compreensão nessa importante jornada. Aos colegas do Grupo de Pesquisa e Interação Cardiopulmonar (GPIC) pela convivência e incentivo, em especial ao colega e amigo Alan Bahr.

Aos pesquisadores, profissionais de saúde, André Kracker Imthon, Ana Claudia Piccolo, Gabriela Joca Marins, Lis Campos Ferreira, Marlise de Castro Ribeiro, Nise Alessandra de Carvalho Souza, Raquel Vassão Araújo e Rodrigo Barbosa Thomaz pelo auxílio na coleta de dados e, comigo, dividir minhas preocupações;

Aos pacientes com esclerose múltipla pela confiança no trabalho, respeito e acreditarem que com nosso trabalho podemos ajudar a melhorar o entendimento da doença;

Aos colegas do Curso de Pós-graduação em Ciências da Saúde pela acolhida, divisão de angústias e companheirismo durante este período, em especial aos que, além de colegas construímos uma amizade: André Imthon, Andrieli Garlet, Augusto Guidoti, Laura Pozzobon e Matheus Ventura;

Aos meus pais Sergio Ricardo Sanches Gonçalves e Marisa Bastos Pereira pela minha formação, educação, amor, paciência e confiança durante toda minha trajetória; à minha irmã Bibiana Pereira Gonçalves pela disponibilidade de sempre; às minhas avós Anita e Alda pelo carinho sempre disponibilizado a mim;

Ao meu namorado William da Silva Denis pelo amor, confiança, apoio, porto seguro e companheirismo nesses anos de união e cumplicidade.

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LISTA DE ABREVIATURAS E SIGLAS

COVID-19	Coronavirus disease 2019
DMT	Disease-modifying therapy
EM	Esclerose múltipla
GAD	Generalized Anxiety Disorder
GAD-7	Generalized Anxiety Disorder-7
HADS	Escala Hospitalar de Ansiedade e Depressão
MS	Multiple sclerosis
pwMS	Patients with multiple sclerosis
TAG	Transtorno de ansiedade generalizada

SUMÁRIO

RESUMO

INTRODUÇÃO: A COVID-19 afetou as regiões brasileiras em tempo e formas diferentes. Sendo um país continental a diferença na ação da COVID-19 pode afetar os pacientes com esclerose múltipla de forma diferente. Até este momento, pouca informação está disponível sobre a incidência de ansiedade em pacientes com esclerose múltipla durante a pandemia da doença de coronavírus 2019 (COVID-19) no Brasil. **OBJETIVO:** Verificar a prevalência do transtorno de ansiedade em pacientes com esclerose múltipla durante a pandemia de COVID-19. **METODOLOGIA:** Este estudo observacional foi baseado em um questionário online conduzido entre primeiro e 31 de agosto de 2020 e respondido pelos pacientes com esclerose múltipla que vivem nas cinco diferentes regiões brasileiras. **RESULTADOS:** Quatrocentos e trinta e seis pacientes com esclerose múltipla participaram do estudo, sendo a maioria mulheres (80.7%), com idades entre 20 e 30 anos. 72.7% dos sujeitos apresentaram algum nível de ansiedade, mais prevalente em mulheres (19%) e pacientes com nível de escolaridade menor que ensino médio completo (25%). Não houve diferença significativa quando consideradas as diferentes regiões brasileiras (p=0.079). **CONCLUSÃO:** O transtorno de ansiedade teve uma alta prevalência em pacientes brasileiros com esclerose múltipla, mas com mesmo comportamento em todas as regiões do país. Dessa forma, sugerimos que as políticas publicas de saúde mental devem alcançar todo o país de forma igualitária.

Palavres-chave: esclerose múltipla; ansiedade; COVID-19.

ABSTRACT

INTRODUTION: The COVID-19 affected Brazilian regions in different times and in different ways. As a continental country, the difference in COVID-19 action may affect pwMS differently. Little information is available regarding the incidence of anxiety in patients with multiple sclerosis (pwMS) during the coronavirus disease 2019 (COVID-19) in Brazil. **OBJECTIVE:** To verify the prevalence of the anxiety disorder in pwMS during the COVID-19 pandemic. **METHODS:** This observational study was based on an online questionnaire conducted between the 1st and 31st August 2020 and answered by pwMS who live in the five different Brazilian regions. **RESULTS:** Four hundred thirty-six pwMS participated in the study, most females (80.7%), aged between 20 and 30 years old. 72.7% of subjects have presented some level of anxiety, more prevalent in females (19%) and patients with high school and below education level (25%). There hasn't been a significant difference when considering the five Brazilian regions (p=0.079). **CONCLUSION:** The anxiety disorder had a high prevalence in Brazilians pwMS, but with the same behavior in all country regions. Therefore, we suggest that the public mental health policies should reach the whole country equally.

Keywords: multiple sclerosis; anxiety; COVID-19.

1 INTRODUCÃO

A esclerose múltipla (EM) é uma doença crônica, de caráter inflamatório, desmielinizante e degenerativo[1,2]. Em torno de 2,5 milhões de pessoas ao redor do mundo são afetadas, sendo que no Brasil a prevalência estimada é de 8,69/100.000 habitantes, apesar de poucos estudos[3]. É a doença neurológica mais comum em jovens adultos[4,5]. A doença incide mais nas mulheres e o início dos sintomas aparece mais frequentemente entre a segunda e terceira década de vida, podendo afetar a saúde e o bem-estar do doente e dos que o rodeiam nos mais diversos aspectos clínicos, psicológicos e sociais, interferindo de forma significativa na qualidade de vida[1,2,4,6,7,8].

Atualmente, o mundo está sofrendo uma pandemia pela doença de coronavírus 2019 (COVID-19), a qual tem afetado a saúde física e mental da população. Coronavírus são vírus respiratórios, da família *coronaviridae*, e algumas espécies podem infectar humanos. Foram isolados em 1937, mas somente em 1965 receberam este nome, devido à aparência de coroa quando visualizados à microscopia[9]. Em dezembro de 2019, na cidade de Wuhan, na China, foi descoberto um novo agente do coronavírus denominado SARS-Cov-2[9]. Este agente é considerado o causador da COVID-19, uma doença com manifestações principalmente respiratórias que pode resultar desde casos assintomáticos até o óbito[9].

Pandemia é por definição “uma epidemia que ocorre em todo o mundo ou sobre uma área muito ampla, cruzando fronteiras internacionais e geralmente afetando um grande número de pessoas”[10]. Em 11 de março de 2020 a Organização Mundial de Saúde passou a caracterizar a COVID-19 como um pandemia[11]. O isolamento social tem sido aplicado como uma estratégia na redução do número de novos casos. Com isso, além do adoecimento físico, a população está exposta a dificuldades financeiras, aumento do desemprego, e afastamento dos familiares e amigos, sendo estes alguns dos problemas que podem ser enfrentados nesse período.

Ansiedade é uma emoção caracterizada por sentimentos de tensão, pensamentos preocupados e mudanças físicas. O transtorno generalizado de ansiedade (TAG) é a existências destas preocupações e sentimentos relacionados a diversas situações e na qual o individuo tem dificuldade de controlá-las[12].

Pacientes com esclerose múltipla possuem uma prevalência de transtornos de ansiedade ao longo da vida entre 22.1%[13] e 35.7%[14], e diante de uma pandemia poucos dados existem para compreender como esses percentuais se comportam. Por exemplo, durante o surto de COVID-19 na Itália encontrou-se uma prevalência de ansiedade de 16.4% de acordo com o State-Trait Anxiety Inventory[15].

Estudos têm encontrado diferentes resultados sobre a prevalência de ansiedade durante a pandemia. Desde aumento da prevalência de ansiedade em pacientes com EM[16,17], até dados que não demonstram alterações[15]. Possivelmente isto depende do momento no qual o estudo foi realizado assim como do tipo de questionário utilizado[18].

Dessa forma, acreditamos que as taxas de ansiedade em pacientes com EM no Brasil sejam mais elevadas, possivelmente, por esta população apresentar maiores preocupações com sua saúde, assim como, preocupações em piorar sua doença devido a COVID-19.

2 JUSTIFICATIVA

Este estudo proporcionará informações relevantes para médicos neurologistas e psiquiatras na tomada de decisão clínica, contribuindo com a literatura acerca do tema, e preenchendo uma lacuna nas evidências do transtorno de ansiedade em pacientes com EM, durante a pandemia do COVID-19.

A EM é um distúrbio desmielinizante progressivo do sistema nervoso central, e é a causa mais comum de deficiência neurológica em adultos jovens e de meia-idade[19]. Em contraste com a grande quantidade de literatura dedicada à depressão em pacientes com esclerose múltipla, escassa atenção tem sido dada aos transtornos de ansiedade. Somente um estudo usou uma entrevista clínica estruturada para avaliar os assuntos e relatou uma prevalência ao longo da vida de 36%[20].

Outros estudos utilizaram avaliações com escalas de avaliação de auto relato, mais comumente o Escala Hospitalar de Ansiedade e Depressão (HADS)[21]. Com limites de corte variando entre uma pontuação de 8 e 10 na HADS, prevalências pontuais de ansiedade variou de 25 a 41%[22,23].

A alta taxa de prevalência de sintomas de ansiedade foi ainda confirmada em um estudo de 95 pacientes que utilizou a escala de avaliação de ansiedade de Hamilton[24]. Embora esses estudos tenham ilustrado que a ansiedade era frequente e clinicamente relevante em pacientes com EM, a maioria tinha limitações significativas. A escassez de pesquisas dedicadas aos transtornos de ansiedade associados a EM presta aos pacientes um desserviço considerável[14].

Os custos sociais, pessoais e financeiros dos transtornos de ansiedade na população em geral são consideráveis[25,26]. Dados preliminares de um estudo de EM sugerem um quadro de ansiedade ligada a queixas mais somáticas, maior disfunção social e aumento de pensamentos suicidas[23]. Isto ressalta a importância de compreender melhor os transtornos de ansiedade na EM, pois sem avaliação perde-se a chance de reduzir a morbidade associada a esta doença incapacitante.

Com a pandemia de COVID-19 os transtornos de ansiedade tornaram-se mais frequentes na população em geral[27], entretanto, não encontramos pesquisas, especificamente, incluindo os pacientes de esclerose múltipla.

Estudos dessa natureza podem auxiliar o processo de conhecimento e impacto do atual quadro de pandemia pela COVID-19 no transtorno de ansiedade

do paciente de esclerose múltipla e serem benéficos aos especialistas que atendem esta parcela da população, no sentido de melhorar a assistência prestada como também no incremento de políticas públicas que tratam desse assunto.

3 REVISÃO DA LITERATURA

3.1 ESCLEROSE MÚLTIPLA

A EM caracteriza-se por ser uma doença crônica, degenerativa e inflamatória que ataca o sistema nervoso central. É uma das principais causas de incapacidade em adultos jovens[28].

Estima-se que afeta em torno de 2,5 milhões de pessoas no mundo[3]. Quanto a prevalência, a EM sofre uma variação de acordo com a etnia e localidade, diminuindo conforme o declínio da latitude[29,30]. Ocorre com maior incidência em países da Europa e América do Norte[31]. A América do Sul apresenta uma baixa taxa de prevalência[32]. No Brasil, as maiores taxas encontram-se nas regiões Sul e Sudeste[33].

As mulheres são aproximadamente duas vezes mais afetadas que os homens[34]. É uma doença que, geralmente, inicia-se entre os 20 e 40 anos de idade, tendo a maior ocorrência de início dos sintomas por volta dos 30 anos, podendo, raramente, ocorrer nos primeiros cinco anos de vida, assim como na sétima década[35].

Ainda considerada uma doença de etiologia desconhecida, a EM apresenta-se como uma desordem heterogênea tanto em suas características clinicas como patológicas[36]. Uma das teorias mais aceitas é que a EM inicia-se como uma doença inflamatória imunomediada caracterizada por linfócitos autorreativos, na sequência dominada pela ativação da micróglia e neurodegeneração crônica[37].

Infiltrados perivasculares de células inflamatórias, desmielinização e perda axonal[38,39,40] são alguns dos marcadores patológicos da doença. Essas alterações são causas das inúmeras formas de apresentação clinica da EM. Fraqueza muscular, espasticidade, hiperreflexia, parestesias, nistagmo, diplopia e neurite optica são os principais sinais e sintomas da doença[4].

A EM pode apresentar exacerbações do quadro inflamatório, conhecida por “surto”, “ataque” ou “recaída”, que se caracteriza por um sintoma neurológico novo ou exacerbação de um sintoma antigo, com duração de pelo menos 24 horas, com ou sem recuperação, na ausência de febre ou infecção[41].

3.1.1 Subtipos

Na dependência da forma de apresentação e curso dos sintomas típicos da doença, a EM caracteriza-se em diferentes fenótipos. Essa distinção torna-se importante para homogeneidade, prognóstico, comunicação entre especialistas e decisão de tratamento[42].

Segundo Lubin et al 2013[2], os fenótipos clínicos da EM seriam:

- Síndrome Clinica Isolada: apresentação de um único sintoma da doença, acompanhado de outros marcadores diagnósticos (alterações típicas na ressonância magnética e/ou bandas oligoclonais)[2];

- Remitente-recorrente: forma mais comum de EM, caracterizada por surtos separados por períodos de remissão[2];

- Secundariamente Progressiva: fase posterior da remitente-recorrente, ocorrendo maior deterioração neurológica[2];

- Primariamente Progressiva: subtipo menos comum, apresenta deterioração neurológica continua desde inicio da doença sem períodos de remissão de sintomas[2].

3.2 ANSIEDADE

A ansiedade é uma sensação causada por resposta funcional, caracterizando-se por um sentimento desagradável, difuso, de preocupação intensa e persistente usualmente acompanhado por sintomas como: cefaleia, palpitações, desconforto no peito e abdome[43,44]. A ansiedade pode ser classificada como um “estado”, quando manifestada em caráter transitório, decorrentes de algum episodio vivenciado pelo individuo, ou como “traço” quando característica constante da personalidade do individuo[45].

Uma pessoa ansiosa pode apresentar uma diversidade de sintomas, variando de cada individuo, não havendo um padrão de manifestação[43]. Sintomas físicos, motores e viscerais tendem a se apresentar juntamente com os sintomas de

medo, incertezas, angústia, podendo afetar no aprendizado, na memória e concentração[46].

Há uma enorme gama de transtornos relacionados a ansiedade. Entre eles estão: fobia especifica, transtorno de ansiedade social, transtorno de pânico, agorafobia, transtorno de ansiedade generalizado[46].

3.2.1 Transtorno de Ansiedade Generalizado

O TAG é caracterizado por preocupações excessivas e persistentes, difícil de controlar, causando sofrimento ou prejuízo significativo ao individuo ocorrendo na maior parte dos dias[46]. É um dos mais comuns transtornos mentais encontrados tanto na parte clinica com na sociedade[47].

Dentre os transtornos de ansiedade o TAG apresenta-se como um dos mais prevalentes, sendo mais encontrado em mulheres, pessoas de menor renda, menor escolaridade e portadores de doenças crônicas[48].

Além da apresentação de preocupação excessiva e persistente – amplamente considerada característica especifica de TAG – sintomas como falta de sono, fadiga, dificuldade de relaxar, dores de cabeça e pescoço são os mais comumente encontrados nos indivíduos acometidos[46].

3.3 ESCALA GAD-7

A escala Transtorno de Ansiedade Generalizada-7 (GAD-7) é uma ferramenta usada amplamente desenvolvida para triagem de TAG[49]. É uma escala breve, de auto relato, na qual o individuo responde sete itens de sintomas de ansiedade generalizada[49]. Cada item apresenta uma escala de quatro pontos com base na frequência com que os indivíduos foram incomodados nas últimas duas semanas. As pontuações totais variam de zero a 21, com as pontuações mais altas referindo-se aos níveis mais altos de gravidade na sintomatologia de TAG[50].

4 OBJETIVOS

4.1 GERAL

Investigar a prevalência de transtornos de ansiedade em pacientes de esclerose múltipla brasileiros durante a pandemia pela COVID-19.

4.2 ESPECÍFICOS

a) Caracterizar dados sociodemográficos da população estudada;

b) Identificar dados clínicos da esclerose múltipla;

c) Avaliar a frequência de pacientes portadores de EM com diagnóstico de COVID-19;

d) Comparar os resultados de transtorno de ansiedade entre as regiões do país.

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6 ARTIGO

TITLE

Anxiety in patients with multiple sclerosis in Brazil during the COVID-19 pandemic

ABSTRACT

Introduction: Little information is available regarding the incidence of anxiety in patients with multiple sclerosis (pwMS) during the coronavirus disease 2019 (COVID-19) in Brazil. The COVID-19 affected Brazilian regions in different times and in different ways. As a continental country, the difference in COVID-19 action may affect pwMS differently.

Objective: To verify the anxiety symptoms in pwMS during the COVID-19 pandemic.

Methods: This observational study was based on an online questionnaire conducted between the 1st and 31st August 2020 and answered by pwMS who live in the five different Brazilian regions.

Results: Four hundred thirty-six pwMS participated in the study, most females (80.7%), aged between 20 and 30 years old. 72.7% of subjects have presented some level of anxiety, more prevalent in females (19%) and patients with high school and below education level (25%). There was not a significant difference of anxiety simptoms among the five Brazilian regions (p=0.079).

Conclusion: The anxiety disorder had a high prevalence in Brazilians pwMS, but with the same behavior in all country regions. Therefore, we suggest that the public mental health policies should reach the whole country equally.

INTRODUCTION

On March 11, 2020, the World Health Organization classified COVID-19 as a pandemic (1). COVID-19 has caused physical damage and alterations in the mental health of the world's population (2,3). However, until recently, mental health in pandemic periods wasn't considered essential and was often neglected (4–6).

An increase of studies on mental health is expected in the next few years, considering a change in healthcare and public health policies(7). Generalized Anxiety Disorder (GAD) is the existence of worries and anxieties related to various situations where the individual has difficulties controlling them(8).

The GAD is the most common cause of mental disorders in the general population, and some studies suggest that in Multiple Sclerosis (MS), it can be more frequent than depression(9,10). In addition, there has been a rise in psychiatric symptoms due to COVID-19 in patients with preexisting chronic diseases (11). However, pwMS haven't explicitly been investigated, even though they've already shown significant vulnerability to neuropsychiatric symptoms(2).

MS is a progressive demyelinating disease of the central nervous system that affects around 2.5 million people worldwide, and in Brazil, the prevalence is estimated at 8.69/100.000 inhabitants(12,13). In addition, pwMS presents several physical and mental neurologic symptoms(14).

Recent studies have found different results on the prevalence of anxiety during the pandemic. While an increase in the prevalence of anxiety in pwMS has been founded(15,16), some data showed no changes(17). Possibly this depends on the moment in which the study was carried out as well as the type of questionnaire used(18).

Thus, we believe that anxiety rates in pwMS in Brazil are higher, possibly because this population presents greater concerns about their health, as well as concerns about worsening their disease due to COVID-19.

Therefore the objective of this study was to verify the prevalence of the anxiety disorder in pwMS during the COVID-19 pandemic in Brazil.

MATERIALS AND METHOD

Study design

This was an observational, descriptive, and cross-sectional study based on an online questionnaire conducted between the 1st and 31st August 2020 and answered by pwMS who live in the five different Brazilian regions: North, South, Northeast, Southeast, and Midwest.

The Ethical Committee of the Universidade Federal de Ciências da Saúde de Porto Alegre approved the study (CAAE 34289120.1.0000.5345). Furthermore, an agreement term was provided to all participants by internet, and all participants have authorized their participation in the research.

We've adopted STROBE guidelines to conduct the paper and the observational studies reports(19).

Participant recruitment

Recruiting took place in the individuals' birth regions through the researchers who were collaborating with the study via MS-related ads, as well as through individual invitations with the following text: "You're being invited to take part in an online research about the view that you, pwMS, are having about your health during the COVID-19 pandemic". The researchers who were in charge were health professionals with expertise on the subject. The eligibility criteria of the subjects were to be at least eighteen years old, diagnosed with MS and to have accepted to participate in the study, and to have read and signed the agreement term.

Calculation of the size of the sample

Three hundred ninety-five estimated participants were used to find a similar correlation to the one observed by Alexandra L. Terrill (2015) between the GAD-7 score and the length of the disease ($r=-0.14$)(9), with a 5% significance and 80% power(9).

Data collection

Data was collected through a questionnaire online, possibly being accessed on smartphones, tablets, and computers. All answers were anonymous.

Two questionnaires were applied: a) a questionnaire with questions related to the sociodemographic profile (6 questions), their MS clinical characteristics (6 questions), and those about COVID-19 (4 questions); b) GAD-7 questionnaire(20).

The GAD-7 was developed like a brief questionnaire to analyze the anxiety symptoms based on the GAD(21). The instrument is based on seven questions with four scores: Likert scale where 0: no days; 1: some days; 2: more than half of days; and 3: almost every day. The final score is the sum of all seven questions (varying from 0 to 21 points). The questionnaire was validated for the general population, the psychiatric population, and also the MS population. The cut points to classify the gravity of the anxiety are: 0-4 = none/normal, 5-9= mild, 10-14= moderate and 15-21=severe(9).

Statistical analysis

Data were analyzed using the SPSS software version 25. The categorical variables were presented in absolute and in percentage frequency.

As the GAD-7 score wasn't normally distributed, nonparametric tests were made. To analyze the GAD-7 with the sociodemographic data, the following tests were used: Mann-Whitney (to evaluate the total score of the GAD-7 and gender), Kruskal-Wallis (to compare GAD-7 in the Brazilian regions and by age). In addition, the chi-square test by Pearson was used to analyze the degrees of GAD-7 and questions related to COVID-19. The significance level of 5% was considered meaningful to all analyses ($p<0.05$).

RESULTS

Four hundred thirty-eight pwMS were invited to participate in the study, and only two didn't sign the agreement term. One hundred sixty-four patients who filled out the questionnaire were from the South region, 149 from the Southeast, 22 from the Midwest, 81 from the Northeast, and 20 from the North.

Sociodemographic data presented in table 1 shows that the sample was 436 pwMS, most were female (80.7%), with ages ranging from 20 to 30 (44%). The predominant ethnic group was white (66.3%), and most were married/stable relationship (54.1%), Postgraduates / Master's or PhDs were the majority (35.1%), and most lived in South and Southeast Brazil (37.6% and 34.2%, respectively).

Table 2 shows the variables related to the clinical characteristics of pwMS, where 80.3% of cases were referred to as a sub-type of relapsing-remitting. In addition, 25% of patients have had MS for 3 to 6 years, 58.3% have been treated by the private health care system. In addition, 88.5% of patients used the disease-modifying therapy (DMT), and most of them (36.9%) have used only one DMT.

Results of the GAD-7 score frequency (mean 8.2±5.5) are demonstrated to the left in figure 1. To the right, it's shown that 72.7% of subjects have presented some level of anxiety: 39.9% mild, 16.3% moderate, and 16.5% severe.

When comparing GAD-7 scores by gender, age, and Brazilian regions using the Mann-Whitney test, it's seen that females have shown higher scores (8.8±5.7) than males (5.9±4.4) with $p<0.001$. We've used the Kruskal Wallis test to verify the scores by age, where patients older than 40 showed lower anxiety scores ($p<0.001$). There hasn't been a significant difference when considering the five Brazilian regions (Kruskal Wallis test). Table 3

When comparing men and women, through Pearson's square, it's noticeable a significant difference ($p=0.001$) where women presented severe levels of anxiety (19.0%) whereas men didn't show signs of anxiety (42.9%). In addition, subjects in their 30-40s were the ones with the most severe anxiety levels (25.3%). Concerning the educational level, subjects with post-graduation showed mild anxiety (47.1%), whereas patients with high school and below had higher levels of severe anxiety (25%), $p = 0.013$ (table 4).

Twenty-one were diagnosed with COVID-19 (table 5), not having any significant difference ($p=0.53$) between having or not anxiety symptoms in its many levels. About the questions that asked related to COVID-19 and the fear of contracting it, where the answers ranged from "totally," "much," "little," "very little," and "no," patients with severe anxiety answered with "total" fear of contracting COVID-19 ($p<0.001$; 31%) and, "little" and "very little" in subjects with no anxiety ($p<0.001$; 33.9% and 50% respectively).

Additionally, patients with severe anxiety were “totally” afraid of dying due to COVID-19 ($p<0.001$; 25.6%), as well as the ones who didn’t have signs of anxiety who replied being “very little” afraid or not afraid at all of dying due to COVID-19 ($p<0.001$; 39.3% and 49.3 %, respectively). The same pattern is noticed in fear of MS getting worse due to COVID-19.

In table 6, we can see that the Midwest, although being represented by only one case of COVID-19 (4.5%), it has replied as being ‘totally’ afraid of their MS getting worse due to COVID-19 (54.5%) when compared to the other regions ($p<0.039$).

DISCUSSION

In this study, we have used a clinical interview to verify anxiety symptoms through self-reports and the GAD-7 to characterize the anxiety disorder and its levels comparing the clinical correlation in the sample of four hundred thirty-six pwMS who live in Brazil, after five months of COVID-19 being classified as a pandemic by WHO.

COVID-19 has affected the mental health of infected patients and the psychosocial health of the non-infected world population, with increases in the numbers of depression, stress, and anxiety(22).

Anxiety occurs when sensations and changes in the homeostasis are perceived, including those related to infectious diseases. These perceptions usually arise in the individuals, but these perceptions become excessive, and the possibility of severe complications to the individual rise in some cases. Lately, this experience has become constant, mainly in events imposed by the presence of COVID-19(23).

If on the one hand, the high levels of stress can generate changes that can be characterized by extreme behaviors like excessive hand washing, social isolation, and panic, which can turn into negative consequences to the person or the society, i.e., in the inadequate use of family financial budgets and the scarcity of resources(23,24). On the other hand, the low level of anxiety can also compromise the safety of the population, i.e., when people minimize the importance of self-care (the use of masks and hand-washing), governments that don’t worry about information campaigns about the disease and care for the population, the adequate isolation, and vaccination, facts that can contribute to the spreading of the virus(25).

That being said, restrictive and preventive measures are fundamental to control the pandemic.

Da Silva et al. (3) have performed a systematic review with meta-analysis of 16 studies involving patients with anxiety disorder related to the COVID-19 pandemic. The total population was 25.779 participants, and 46% of these have presented some anxiety symptoms. The analysis of the subgroup of the study population showed that 52.6% of the general population (IC 95% 42.0-63.2%) had a higher prevalence of anxiety symptoms, followed by health professional doctors with 49.9% (IC 95% 15.4–84.4%) and infected patients with 8.0%. However, the results have shown that none of the ages (β=-0.027, p=0.060) or genders (β=0.406, p=0.562) were significant moderators of the prevalence of anxiety symptoms. The authors suggest that the anxiety disorder can be related to social isolation or the isolation determined by the governments, by fear caused due to the severity of the disease, or even a risk of crisis due to economic and financial impact or even the fear of life loss.

As far as we are concerned, our study is the first to specifically deal with the frequency of the anxiety disorder in pwMS during the COVID-19 pandemic in Brazil. Furthermore, the profile of the researched subjects has shown that the most significant percentage was in white women, between 30 and 40, which has agreed with many literature studies regarding MS(26).

On the other hand, men have presented a significantly lower anxiety disorder than women(11). A study by Korostil e Feinstein (2007)(27) that evaluated 140 pwMS hasn’t found any gender differences concerning any levels of severity of MS.

The study by Korostil e Feinstein (2007)(27) suggests that the patients’ perceptions of the increase of the psychosocial stressors and the decrease of the social support were significantly related to the development of the anxiety disorder. This data has also shown that the diagnosis of an anxiety disorder is also connected to suicidal intentions and auto-mutilation attempts. Therefore, the authors highlight the necessity of an early diagnosis and treatment. It’s also important to point out that anxiety disorder increases depression in two-thirds of the patients(27).

In the present study, most patients reported a relapsing-remittent disease for over three years, ages between 30 and 40, employed and with post-graduate levels.

In the Wang et al. (2020)(11) study, people with a student status were associated with anxiety compared to those employed. Our research has revealed

that subjects with a higher education level showed higher levels of anxiety. Prior epidemiologic studies have reported that students have suffered a psychological impact during the pandemic with higher stress, anxiety, and depression(28).

The uncertainty of the academic progression can have a side effect on the mental health of the academy students. So, it's essential that during the pandemic, the educational authorities base themselves on online applications to offer learning activities(29). Furthermore, as the youngsters are more receptive to the digital world, i.e., with cell phone applications(30), the health teams could give online lectures related to psychoeducation or even offer individual psychological interventions.

The COVID-19 pandemic has changed people's routines and behaviors, social lives, work, and personal care a lot, but we've noticed that most patients (88.5%) have continuously used disease modification therapy (DMT).

In our study, 72.7% of the subjects presented some anxiety: 39.7% mild, 16.3% moderate, and 16.7% severe. However, an online study conducted between January 31st and February 2nd, 2020, with the general population of China that had as an objective the verification of the levels of psychological impact, anxiety, depression, and stress during the initial phase of the COVID-19 outbreak, showed that to an anxiety subscale, 770 (63.6%) were considered as to having normal punctuation; 91 (7.5%) had mild anxiety; 247 (20.4%) moderate anxiety; and 102 (8.4%) severe and extremely severe anxiety(11).

In another study(27) that evaluated 140 pwMS, 35.7% of the sample had a diagnosis of anxiety disorder throughout life, and 14% were suffering from it at the time of the study. Thus, the prevalence of the anxiety disorder rate is way higher than what had already been recorded in the literature, which was 25% throughout the population's lives, reported by the National Comorbidity Study(31).

Although comparisons between diseases should be made cautiously, rates of anxiety in MS are also higher than estimates in general chronic cases(32), or specific chronic diseases where high levels of anxiety can be found like diabetes(33), chronic obstructive pulmonary disease(34) and rheumatoid arthritis(35). Additionally, in comparison to other neurologic disorders, the Korostil and Feinstein (2007)(27) study exceeds the observed in patients with epilepsy(36), being comparable to patients with untreatable convulsions(37). Still, it's slightly lower than the 40% observed in Parkinson's disease(38).

As men, in their majority, don't show anxiety (42.9%), it can be thought that they'd be in a more comfortable financial situation because they have already finished their education. But, in contrast, the young adults are still building their futures, with many uncertainties like whether they'll finish their studies and if they're employed, whether they could lose their jobs, or if the companies they work for will go bankrupt, or living costs will get higher, or there'll be a lack of opportunities and so on.

Unquestionably, the COVID-19 pandemic has brought many worries to pwMS, including the fear of coming down with COVID-19 and dying from it, and worsening their MS condition due to the infection. Our research has shown 21 cases of COVID-19. In addition, a Brazilian National study showed an incidence in pwMS of 27.7/10.000 patients in a similar period, similar to the general incidence in the Brazilian population(39).

Our study has shown that patients with severe anxiety were totally afraid of contracting COVID-19, whereas those with no anxiety were a little or very little afraid of getting it. This may have occurred because these fears may already be symptoms of anxiety.

Most interviewees believed that it would be very probable or there would be some probability of surviving COVID-19 if infected. In the same way, fear appears as "total" in severe anxiety situations. Maybe this happens because patients with severe anxiety are more alert to the disease situations. The Wang et al. (11) study has demonstrated that most of the interviewees (> 70%) were worried about the possibility of their families being infected by COVID-19, and they believed they'd survive if infected.

We've found in our study that in the different regions of Brazil, although very distinct in ethical and cultural terms, the anxiety disorder of the pwMS didn't show any significant differences. So, in this way, all are prone to having mental health problems during the pandemic.

The COVID-19 pandemic is a worldwide phenomenon that has affected and still affects pwMS, who, among all clinical approaches, the evaluation of their mental health lacks special attention.

The two most important limitations in the present study hides in the data gathering stage where information is obtained from patients subjectively by online questionnaire

and that no information has been collected previously on the mental health from the sample.

CONCLUSION

The COVID-19 pandemic is a worldwide phenomenon that has affected and still affects the general population and, in particular, pwMS. The evidence from this present study suggests that anxiety disorder had a prevalence of 72.7% of subjects.

These results have clinical and political implications on pwMS. It’s important to highlight that in clinical approaches, the evaluation of mental health has special attention.

Data suggests that students have had the highest levels of anxiety. The uncertainty and the potential negative impact on the academic progression may have a side effect on the students' mental health. As the youngsters are more receptive to the digital world, the health authorities must identify, evaluate and offer psychological interventions to these patients.

PwMS from the different regions in Brazil have shown the same behavior towards anxiety. This way, we suggest that the public mental health policies should reach the whole country equally.

The fact that no information has been collected previously on the mental health from the sample results in the negative quantification of how much the COVID-19 pandemic has contributed to the worsening of anxiety symptoms. So other studies must be conducted to elucidate this matter.

As the epidemic continues, the health government system must make the health teams aware of the prevalence of anxiety in pwMS and its early clinical intervention.

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TABLES

Table 1 - Socio-demographic data n = 436

Characteristics	*n (%)*
Age	
18 - 20	83 (19)
20 - 30	192 (44)
30 - 40	99 (22.7)
40 - 50	44 (10.1)
> 50	18 (4.1)
Gender	
Male	84 (19.3)
Female	352 (80.7)
Ethnicity	
White	289 (66.3)
Non-White	147 (33.7)
Marrital Status	
Single	159 (36.3)
Married / Stable Union	236 (54.1)
Divorced	41 (9.4)
Education Level	
High School and Below	148 (33.9)
University Degree	135 (31)
Postgraduate/Master's/PhD	153 (35.1)
Employed	
Yes	245 (56.2)
No	191 (43.8)
Region	
South	164 (37.6)
Southeast	149 (34.2)
Mid-west	22 (5)
Northeast	81 (18.6)
North	20 (4.6)

Table 2 - Clinical characteristics of patients (n = 436)

MS Type *n (%)*	
Relapsing-Remitting	350 (80.3)
Secondary Progressive	19 (4.4)
Primary Progressive	12 (2.8)
Missing	55 (12.6)
MS Duration (years) *n (%)*	
< 1	41 (9.4)
1 - 3	93 (21.3)
3 - 6	109 (25)
6 - 10	80 (18.3)
10 - 15	65 (14.9)
> 15	48 (11)
Health Care System *n (%)*	
Private	254 (58.3)
Public	182 (41.7)
Disease-modifying Therapy (DMT) *n (%)*	
Yes	386 (88.5)
No	55 (11.5)
Numbers of DMT *n (%)*	
One	160 (36.9)
Two	142 (32.7)
Three	65 (15)
More than three	57 (13.1)
No medication	10 (2.3)

Table 3 – Differences between GAD-7 total score by age, gender, and region of Brazil.

Characteristic	*M (SD)*	p-value
Gender		
Female	8.8 (5.7) *	< 0.001[⊥]
Male	5.9 (4.4)	
Age		
18 - 20	8.9 (5.7)	< 0.001[Y]
20 - 30	8.5 (5.4)	
30 - 40	9.3 (6.0)	
40 - 50	5.3 (4.6) *	
> 50	3.6 (2.3) *	
Region		
South	7.3 (5.0)	0.089[Y]
Southeast	9.0 (5.9)	
Mid-west	9.5 (6.4)	
Northeast	8.5 (5.7)	
North	7.4 (6.0)	
Education Level		
High School and Below	9.3 (6.2)	0.050[Y]
University Degree	8.1 (5.4)	
Postgraduate/Master's/PhD	7.3 (5.0)	

M = mean; SD = standard deviation; * = statistical difference; [⊥] = Mann-Whitney test; [Y] = Kruskal Wallis test

Table 4 – Differences between gender and age about categorical GAD-7.

	Categorical GAD-7				p-value
	None *n(%)*	Mild *n(%)*	Moderate *n(%)*	Severe *n(%)*	
Gender					
Female	83 (23.6)	142 (40.3)	60 (17)	67 (19,0) *	0.001
Male	36 (42.9) *	32 (38.1)	11 (13.1)	5 (6)	
Age					
18 - 20	16 (19.3)	35 (42.2)	16 (19.3)	16 (19.3)	< 0.001
20 - 30	49 (25.5)	77 (40.1)	38 (19.8)	28 (14.6)	
30 - 40	21 (21.2)	39 (39.4)	14 (14.1)	25 (25.3) *	
40 - 50	22 (50) *	16 (36.4)	3 (6.8)	3 (6.8)	
> 50	11 (61.1) *	7 (38.9)	0 (0)	0 (0)	
Education Level					
High School and Below	37 (25)	52 (35.1)	22 (14.9)	37 (25) *	0.013
University Degree	38 (28.1)	50 (37.0)	27 (20)	20 (14.8)	
Postgraduate/Master's/PhD	44 (28.8)	72 (47.1) *	22 (14.4)	15 (9.8)	

* = statistical difference; Pearson Chi-Square test

Table 5 – Differences between questions about COVID-19 and categorical GAD-7

	Categorical GAD-7				p-value
	None *n(%)*	Mild *n(%)*	Moderate *n(%)*	Severe *n(%)*	
Did you have a confirmed COVID-19 diagnosis?					
Yes	5 (23.8)	6 (28.6)	5 (23.8)	5 (23.8)	0.53
Are you afraid of contracting COVID-19?					
Totally	9 (10.3%)	33 (37.9)	18 (2.7)	27 (31) *	
Much	34 (22.4)	65 (42.8)	31 (20.4)	22 (14.5)	< 0.001
Little	43 (33.9) *	53 (41.7)	16 (12.6)	15 (11.8)	
Very little	21 (50) *	15 (35.7)	2 (4.8)	4 (9.5)	
No	12 (42.9)	8 (28.6)	4 (14.3)	4 (14.3)	
Are you afraid of dying for COVID-19?					
Totally	11 (13.4)	31 (37.8)	19 (23.2)	21 (25.6) *	
Much	24 (21.4)	49 (43.8)	19 (17)	20 (17.9)	< 0.001
Little	24 (22.2)	46 (42.6)	20 (18.5)	18 (16.7)	
Very little	24 (39.3) *	25 (41)	5 (8.2)	7 (11.5)	
No	36 (49.3) *	23 (31.5)	8 (11)	6 (8.2)	
Are you afraid that COVID-19 may worsen your condition of multiple sclerosis?					
Totally	15 (13)	44 (38.3)	24 (20.9)	32 (27.8) *	
Much	26 (21.3)	50 (41)	23 (18.9)	23 (18.9)	< 0.001
Little	29 (27.9)	47 (45.2)	18 (17.3)	10 (9.6)	
Very little	20 (48.8) *	18 (43.9)	0 (0)	3 (7.3)	
No	29 (53.7) *	15 (27.8)	6 (11.1)	4 (7.4)	

* = statistical difference; Pearson Chi-Square test

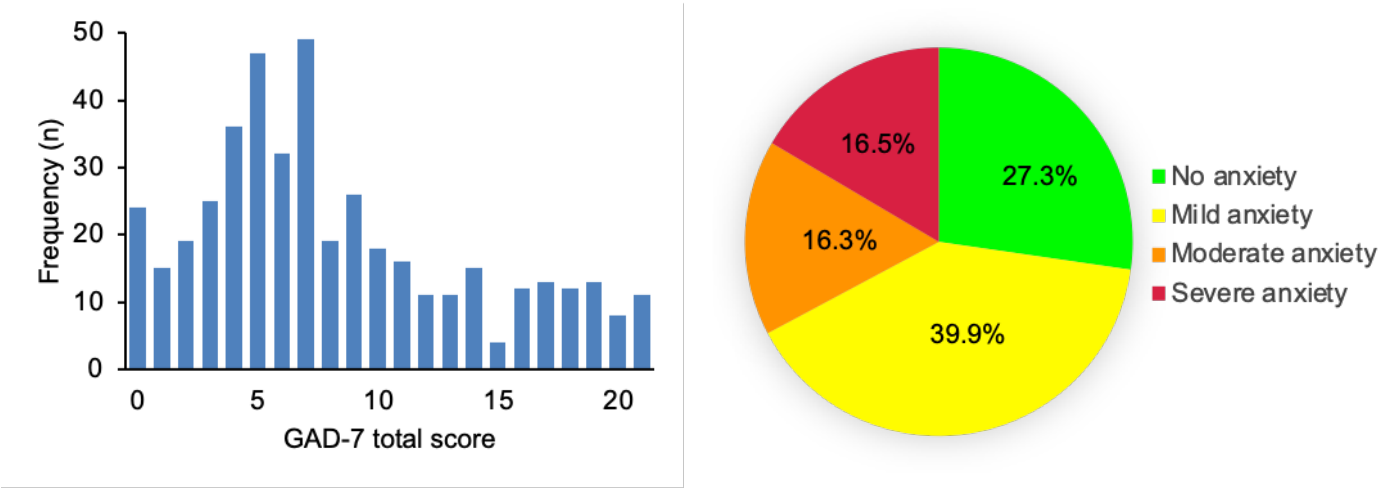
Table 6 - Differences between questions about COVID-19 and region of Brazil

	Region					p-value
	South *n(%)*	Southeast *n(%)*	Mid West *n(%)*	Northeast *n(%)*	North *n(%)*	
Did you have a confirmed COVID-19 diagnosis? Yes	6 (3.7)	7 (4.7)	1 (4.5)	7 (8.6)	0 (0)	0.39
Are you afraid that COVID-19 may worsen your condition of multiple sclerosis?						
Totally	34 (20.7)	37 (24.8)	12 (54.5) *	24 (29.6)	8 (40)	
Much	45 (27.4)	50 (33.6)	1 (4.5)	25 (30.9)	1 (5)	0.039
Little	44 (26.8)	29 (19.5)	7 (31.8)	17 (21)	7 (35)	
Very little	18 (11)	14 (9.4)	1 (4.5)	6 (7.4)	2 (10)	
No	23 (14)	19 (12/8)	1 (4.5)	9 (11.1)	2 (10)	

* = statistical difference; Pearson Chi-Square test

FIGURE

Figure 1 - GAD-7 summed total scores (left) and GAD-7 categorical prevalence (right)



7 CONCLUSÃO

A alta taxa de prevalência encontrada de ansiedade em pacientes com EM durante a pandemia de COVID-19 nos reforçou a importância de ter realizado o estudo.

Verificar o perfil dos pacientes mais acometidos (mulheres, jovens, estudantes) ajudar a pensar em perspectivas e direcionar um tratamento mais adequado a estes grupos na busca de reconhecer precocemente a doença e agilizar o tratamento evitando dano maior aos pacientes.

Ao encontrar o dado que não há diferença significativa entre os níveis de ansiedade nas diferentes regiões brasileiras, apesar das grandes culturais, nos faz crer que politicas publicas de saúde mental possam se adotadas de forma semelhante na busca e tratamento destes pacientes.

Como a pandemia continua, esperamos que este estudo possa ter contribuído para entender algumas questões sobre a ansiedade em pacientes com esclerose múltipla neste momento e vislumbrar novos estudo e medidas que possam acrescentar mais dados a esta literatura ainda pouco aprofundada.

8 ANEXOS

ANEXO 1 – APROVAÇÃO NO COMITÊ DE ÉTICA

UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Percepção da saúde mental do portador de esclerose múltipla durante pandemia de COVID-19 no Brasil.

Pesquisador: Pedro Dal Lago

Área Temática:

Versão: 2

CAAE: 34289120.1.0000.5345

Instituição Proponente: Universidade Federal de Ciências da Saúde de Porto Alegre

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 4.166.007

Apresentação do Projeto:

Trata-se de um estudo transversal com um questionário online para indivíduos brasileiros portadores de esclerose múltipla, com o objetivo de investigar a presença de sintomas ansiosos e depressivos.

Objetivo da Pesquisa:

Objetivo Geral: Investigar a presença de sintomas ansiosos e depressivos em pacientes portadores de esclerose múltipla brasileiros durante a pandemia pela COVID-19.

Objetivos Específicos: - Caracterizar dados sociodemográficos da população estudada; - Descrever formas clínicas da esclerose múltipla e tratamentos realizados pelos pacientes; - Avaliar a frequência de pacientes com sintomas sugestivos de COVID-19; -Caracterizar os sintomas de ansiedade e depressão e fatores a eles associados; - Comparar os resultados entre as regiões do país.

Avaliação dos Riscos e Benefícios:

Riscos mínimos. Apesar de poder ocorrer algum desconforto ao responder alguma das questões apresentadas, o participante, se preferir, poderá desistir de responder mesmo após ter iniciado o questionário.

Benefícios: Participar de uma pesquisa nacional que visa reconhecer o atual panorama da saúde

Endereço: Rua Sarmento Leite ,245
Bairro: Sarmento **CEP:** 90.050-170
UF: RS **Município:** PORTO ALEGRE
Telefone: (51)3303-8804 **E-mail:** cep@ufcspa.edu.br

mental do portador de Esclerose Múltipla no Brasil no contexto da pandemia de COVID-19 com intuito de, a partir dos resultados, planejar medidas de suporte psicológico para esses pacientes em escala nacional.

Comentários e Considerações sobre a Pesquisa:

Todas as pendências foram atendidas.

Considerações sobre os Termos de apresentação obrigatória:

Todos os termos de apresentação obrigatória foram apresentados.

Conclusões ou Pendências e Lista de Inadequações:

Todas as pendências foram atendidas.

Considerações Finais a critério do CEP:

De acordo com o parecer do Relator.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1583279.pdf	06/07/2020 18:57:31		Aceito
Outros	Carta_Resposta.pdf	06/07/2020 18:56:13	RICARDO PEREIRA GONCALVES	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.pdf	06/07/2020 14:24:24	RICARDO PEREIRA GONCALVES	Aceito
Outros	Questionario.pdf	06/07/2020 14:24:12	RICARDO PEREIRA GONCALVES	Aceito
Projeto Detalhado / Brochura Investigador	Projeto.pdf	06/07/2020 14:21:38	RICARDO PEREIRA GONCALVES	Aceito
Outros	Termo_relatorio.pdf	29/06/2020 20:42:38	RICARDO PEREIRA GONCALVES	Aceito
Folha de Rosto	Folha_de_Rosto.pdf	25/06/2020 09:48:56	RICARDO PEREIRA GONCALVES	Aceito

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE

Não

PORTO ALEGRE, 21 de Julho de 2020

Assinado por:
Fernanda Bordignon Nunes
(Coordenador(a))

Endereço: Rua Sarmento Leite ,245
Bairro: Sarmento **CEP:** 90.050-170
UF: RS **Município:** PORTO ALEGRE
Telefone: (51)3303-8804 **E-mail:** cep@ufcspa.edu.br

ANEXO 2 – TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Termo de Consentimento Livre Esclarecido

Projeto de Pesquisa: Percepção da saúde mental do portador de Esclerose Múltipla durante pandemia de COVID-19 no Brasil.

Você está sendo convidado(a) a participar desta pesquisa de forma totalmente voluntária. É muito importante que compreenda as informações contidas neste documento. Você tem todo o direito de desistir de participar desta pesquisa a qualquer momento, sem penalidade nenhuma. Os pesquisadores estão prontos para tirar quaisquer dúvidas que surjam a qualquer momento de sua participação.

Durante situações de epidemias pode ser observado impacto na saúde mental. Entretanto, o foco das pesquisas tem sido o combate do agente infeccioso, e questões relacionadas a sintomas de sofrimento emocional vêm sendo negligenciadas.

O objetivo desta pesquisa é avaliar a percepção que você, portador de esclerose múltipla, está tendo sobre a sua saúde mental neste período de pandemia pela COVID-19, como tem se sentido e suas preocupações acerca deste quadro atual.

Caso aceite participar dessa pesquisa, você deverá responder um questionário online com perguntas sobre você, suas atividades cotidianas, sua doença esclerose múltipla e sobre seu estado emocional frente à pandemia pela COVID-19. Os questionários serão respondidos anonimamente. **Destacamos a importância de guardar em seus arquivos uma cópia do documento deste registro de consentimento. Caso prefira, pode solicitar também uma via assinada pelos pesquisadores pelo e-mail avidacomesclerosemultipla@yahoo.com.**

Em todas as etapas da pesquisa será seguida a Resolução 510/2016 do CNS. Esta pesquisa contribuirá para um maior conhecimento sobre a repercussão psíquica da quarentena e isolamento social perante a pandemia do COVID-19 nos pacientes portadores de esclerose múltipla, e apresentará dados que evidenciam (ou não) a necessidade de ampliação da rede de atendimento em saúde mental, trazendo benefício à população.

O estudo é considerado com riscos mínimos para os envolvidos na pesquisa, tais como constrangimento, visto que algumas perguntas realizadas podem remeter a algum desconforto, evocar sentimentos ou lembranças desagradáveis ou, até mesmo, trazer um certo cansaço após respondê-las. Asseguramos que você não será identificado(a), e que será mantido o caráter confidencial da informação relacionada à sua privacidade, garantindo anonimato, sigilo e confidencialidade dos dados. A sua participação é voluntária e você poderá interrompê-la a qualquer momento sem que isso lhe cause nenhum problema, dano ou constrangimento. Seu consentimento em participar ocorrerá mediante concordância ou assinatura do registro de consentimento livre e esclarecido. Não existirão despesas ou compensações pessoais para o participante, e não haverá compensação financeira relacionada à sua participação.

Ao final da pesquisa nos comprometemos em divulgar os resultados da pesquisa sob a forma de artigo científico a ser submetido para publicação, bem como por meio de informe através do site https://avidacomesclerosemultipla3.webnode.com para que você tenha acesso também ao dados encontrados por meio do questionário respondido. De modo semelhante, acrescentaremos no informe possibilidades de ajuda psicológica, como telefone do Centro de Valorização da Vida (CVV) – 188. Caso necessite, fique à vontade para nos contactar pelo e-mail avidacomesclerosemultipla@yahoo.com.

Esta pesquisa foi submetida para aprovação pelo Comitê de Ética e Pesquisa da Universidade Federal de Ciências da Saúde de Porto Alegre sendo que o contato pode ser realizado através do fone (51) 3303-8804 e/ou na Rua Sarmento Leite 245.

Os pesquisadores responsáveis por esse projeto são André Kracker Imthon, Ana Claudia Piccolo, Gabriela Joca Marins, Lis Campos Ferreira, Marlise de Castro Ribeiro, Nise Alessandra de Carvalho Souza, Raquel Vassão Araújo, Ricardo Pereira Gonçalves, Rodrigo Barbosa Thomaz e Pedro Dal Lago, que estão à disposição para maiores esclarecimentos pelo email: avidacomesclerosemultipla@yahoo.com ou pelo fone: (54) 30390319. Solicitamos a sua autorização para utilizarmos as informações obtidas na pesquisa e, desde já, agradecemos e nos colocamos à disposição para quaisquer esclarecimentos.

Eu_____, RG_____, tendo recebido as informações acima, concordo em participar.

Porto Alegre/RS, _____de _____ de _____.

_____

Assinatura do sujeito da pesquisa

_____

Assinatura do pesquisador

ANEXO 3 – QUESTIONÁRIO SÓCIODEMOGRÁFICO E ESTADO CLÍNICO

Percepção da saúde mental do portador de esclerose múltipla durante pandemia de COVID-19 no Brasil.

Você está sendo convidado(a) a participar de uma pesquisa online sobre a visão que você, portador de esclerose múltipla, está tendo sobre sua saúde durante esta pandemia pela COVID-19. Os pesquisadores responsáveis são os neurologistas Ana Claudia Piccolo, Gabriela Joca Marins, Lis Campos Ferreira, Marlise de Castro Ribeiro, Nise Alessandra de Carvalho Souza, Raquel Vassão Araújo, Ricardo Pereira Gonçalves (avidacomesclerosemultipla@yahoo.com), Rodrigo Barbosa Thomaz e Pedro Dal Lago. Essa pesquisa busca dados que serão apresentados de forma consolidada, e os pesquisadores supracitados asseguram a garantia de confidencialidade com relação aos participantes.

*Obrigatório

Termo de Consentimento Livre e Esclarecido (TCLE)

Você pode copiar e gravar a foto abaixo e guardá-la com você.

1. Após leitura do TCLE abaixo, você concorda em participar da pesquisa? *

Termo de Consentimento Livre Esclarecido

Projeto de Pesquisa: Percepção da saúde mental do brasileiro portador de esclerose múltipla durante pandemia de covid-19

Você está sendo convidado(a) a participar desta pesquisa de forma totalmente voluntária. É muito importante que compreenda as informações contidas neste documento. Você tem todo o direito de desistir de participar desta pesquisa a qualquer momento, sem penalidade nenhuma. Os pesquisadores estão prontos para tirar quaisquer dúvidas que surjam a qualquer momento de sua participação.

Durante situações de epidemias pode ser observado impacto na saúde mental. Entretanto, o foco das pesquisas tem sido o combate do agente infeccioso, e questões relacionadas a sintomas de sofrimento emocional vêm sendo negligenciadas.

O objetivo desta pesquisa é avaliar a percepção que você, portador de esclerose múltipla, está tendo sobre a sua saúde mental neste período de pandemia pela COVID-19, como tem se sentido e suas preocupações acerca deste quadro atual.

Caso aceite participar dessa pesquisa, você deverá responder um questionário online com perguntas sobre você, suas atividades cotidianas, sua doença esclerose multipla e sobre seu estado emocional frente à pandemia pela COVID-19. Os questionários serão respondidos anonimamente.

Esta pesquisa contribuirá para um maior conhecimento sobre a repercussão psíquica da quarentena e isolamento social perante a pandemia do COVID-19 nos pacientes portadores de esclerose múltipla, e apresentará dados que evidenciam (ou não) a necessidade de ampliação da rede de atendimento em saúde mental, trazendo benefício à população.

Ao final da pesquisa os resultados serão disponibilizados através do site https://avidacomesclerosemultipla3.webnode.com para que você tenha acesso também ao dados encontrados por meio do questionário respondido.

O fato de responder algumas dessas perguntas pode lhe causar constrangimento, entretanto garantimos que as informações dessa pesquisa serão mantidas em sigilo, sendo apenas utilizadas de forma científica e anônima.

Não existirão despesas ou compensações pessoais para o participante, e não haverá compensação financeira relacionada à sua participação.

Os pesquisadores responsáveis por esse projeto são Ana Claudia Piccolo, Gabriela Joca Marins, Lis Campos Ferreira, Marlise de Castro Ribeiro, Nise Alessandra de Carvalho Souza, Raquel Araújo Vassão, Ricardo Pereira Gonçalves e Rodrigo Barbosa Thomaz, que estão à disposição para maiores esclarecimentos pelo email: neuro.dr.ricardo@sierrasalut.com ou pelo fone: (54) 30390319.

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

As questões abaixo são para sabermos um pouco sobre você.

Não esqueça que o formulário é sigiloso, por isso fique à vontade para responder o que realmente sente sobre a pergunta.

2. Qual sua faixa etária? *

Marcar apenas uma oval.

- ◯ 18 - 20 anos
- ◯ 20 - 30 anos
- ◯ 30 - 40 anos
- ◯ 40 - 50 anos
- ◯ 50 - 60 anos
- ◯ Acima de 60 anos

3. Qual a região do Brasil que você vive? *

Marcar apenas uma oval.

- ◯ Norte
- ◯ Nordeste
- ◯ Centro-Oeste
- ◯ Sudeste
- ◯ Sul

4. Qual o seu sexo declarado ao nascer? *

Marcar apenas uma oval.

- ◯ Feminino
- ◯ Masculino

5. Com qual gênero você se identifica? *

Marcar apenas uma oval.

- ◯ Feminino
- ◯ Masculino
- ◯ Outro: _____

6. Qual sua orientação sexual? *

Marcar apenas uma oval.

- ◯ Heterossexual
- ◯ Homossexual
- ◯ Outro: _____

7. Como você se vê em relação à sua etnia? *

Marcar apenas uma oval.

- ◯ Amarela
- ◯ Branca
- ◯ Indígena
- ◯ Parda
- ◯ Preta
- ◯ Outro: _____

8. Qual seu estado civil? *

Marcar apenas uma oval.

- ◯ Solteiro(a)
- ◯ Casado(a) / União estável
- ◯ Separado(a) / Divorciado(a)
- ◯ Viúvo(a)

9. Você tem filhos? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

10. Com quem você mora? *

Marcar apenas uma oval.

- ◯ Com cônjuge/companheiro(a)
- ◯ Com família
- ◯ Com outras pessoas
- ◯ Sozinho(a)

11. Você tem animal de estimação? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

12. Qual seu grau de escolaridade? *

Marcar apenas uma oval.

- ◯ Ensino fundamental incompleto
- ◯ Ensino fundamental completo
- ◯ Ensino médio incompleto
- ◯ Ensino médio completo
- ◯ Ensino superior incompleto
- ◯ Ensino superior completo
- ◯ Especialização
- ◯ Mestrado
- ◯ Doutorado
- ◯ Pós-doutorado
- ◯ Outro: _____

13. Você esta empregado? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

14. Qual sua renda familiar mensal? *

Marcar apenas uma oval.

- ◯ Abaixo de 2 salários mínimo (Abaixo de R$ 2.090,00)
- ◯ De 2 a 4 salários mínimo (De R$ 2.090,00 a 4.179,99)
- ◯ De 4 a 10 salários mínimo (De R$ 4.180,00 a 10.449,99)
- ◯ De 10 a 20 salários mínimo (De R$ 10.450,00 a 20.900,00)
- ◯ Acima de 20 salários mínimo (Acima de R$ 20.900,00)

15. Qual sua religião? *

Marcar apenas uma oval.

- ◯ Católica
- ◯ Evangélica
- ◯ Espírita
- ◯ Umbanda
- ◯ Candomblé
- ◯ Judaísmo
- ◯ Muçulmana
- ◯ Budismo / Zen-Budismo
- ◯ Hinduismo
- ◯ Sem religião específica, mas espiritualizada
- ◯ Sem religião, ateu ou agnóstico
- ◯ Outro: _____

Agora queremos saber sobre a Esclerose Múltipla

16. Qual é o sub tipo da sua doença? *

Marcar apenas uma oval.

- ◯ Remitente recorrente
- ◯ Secundariamente progressiva
- ◯ Primariamente progressiva
- ◯ Não sei

17. Quanto tempo você tem de diagnóstico de esclerose múltipla? *

Marcar apenas uma oval.

- ◯ Menos de 1 ano
- ◯ De 1 a 3 anos
- ◯ De 3 a 6 anos
- ◯ De 6 a 10 anos
- ◯ De 10 a 15 anos
- ◯ Acima de 15 anos

18. Você faz acompanhamento da sua doença por qual dos seguinte serviços de saúde? *

Marcar apenas uma oval.

- ◯ Sistema Único de Saúde (SUS)
- ◯ Convênio (Plano de saúde)
- ◯ Particular

19. Você está em uso de medicação para tratar esclerose múltipla? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

20. Quantas medicações você ja fez uso para tratar a esclerose múltipla? *

Marcar apenas uma oval.

- ◯ Uma
- ◯ Duas
- ◯ Três
- ◯ Mais de três
- ◯ Não me lembro
- ◯ Não uso medicação

21. Qual a sua medicação atual? *

Marcar apenas uma oval.

- ◯ Acetato de glatiramer
- ◯ Alentuzumabe
- ◯ Azatioprina
- ◯ Betainterferona 1a 30mcg
- ◯ Betainterferona 1a 22mcg
- ◯ Betainterferona 1a 44mcg
- ◯ Betainterferona 1b 300mcg
- ◯ Cladribina
- ◯ Fingolimode
- ◯ Fumarato de dimetila
- ◯ Natalizumabe
- ◯ Ocrelizumabe
- ◯ Teriflunomida
- ◯ Outro: _____

Algumas perguntas sobre como você tem passado neste período de pandemia pela COVID-19

22. Como você avalia sua qualidade de vida nos últimos dois meses? *

Marcar apenas uma oval.

- ◯ Péssima
- ◯ Ruim
- ◯ Mediana
- ◯ Boa
- ◯ Excelente

23. O quanto você acredita que a pandemia pela COVID-19 pode ter afetado sua qualidade d vida? *

Marcar apenas uma oval.

- ◯ Muito pouco
- ◯ Pouco
- ◯ Nada
- ◯ Muito
- ◯ Totalmente

24. Você acredita que sua vida vai mudar após esta pandemia? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

25. Se sim, de que forma você acha que sua vida possa mudar?

_____

_____

_____

_____

_____

26. O quanto sua crença religiosa ajuda você a se sentir bem durante a pandemia? *

Marcar apenas uma oval.

- ◯ Muito pouco
- ◯ Pouco
- ◯ Nada
- ◯ Muito
- ◯ Totalmente

27. Você está praticando o isolamento social? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não
- ◯ Parcialmente (saindo somente para mercado/farmácia/hospital)

28. Você conta com uma rede de apoio para alguma necessidade específica neste período (i
ao mercado, ir à farmácia por você)? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

29. Você está praticando atividade física? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

30. Marque o(s) sintoma(s) que você vem sentindo nos últimos dois meses: *

Marque todas que se aplicam.

- [ ] Insônia (menos sono que o normal)
- [ ] Mais sono que o normal
- [ ] Choro fácil
- [ ] Tristeza persistente
- [ ] Desmotivação
- [ ] Alucinações (vendo ou ouvindo coisas que outras pessoas não vêem nem ouvem)
- [ ] Redução do apetite
- [ ] Aumento do apetite
- [ ] Irritabilidade
- [ ] Palpitação
- [ ] Sudorese
- [ ] Sensação de falta de ar
- [ ] Redução da energia / fadiga
- [ ] Disfunção sexual (perda da libido, disfunção erétil)
- [ ] Medo
- [ ] Sensação que a vida está andando para trás
- [ ] Culpa
- [ ] Vontade de morrer
- [ ] Nenhum dos sintomas

Outro: [ ] _____

31. Qual é a sua fonte de renda atual? *

Marcar apenas uma oval.

- ◯ Profissional liberal / autônomo
- ◯ Emprego formal (carteira assinada)
- ◯ Servidor Público
- ◯ Emprego informal
- ◯ Tenho empresa / sociedade de prestação de serviço
- ◯ Sou aposentado(a) pelo INSS
- ◯ Não tenho renda

32. Você perdeu seu emprego? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não
- ◯ Não tenho emprego formal

33. Você está trabalhando presencialmente? *

Marcar apenas uma oval.

- ◯ Sim, continuo trabalhando presencialmente
- ◯ Não, estou trabalhando à distância / trabalhando de casa (home office)
- ◯ Não, estou afastado totalmente do trabalho
- ◯ Não, fui demitido
- ◯ Não trabalho

34. Sua renda foi afetada neste período de pandemia? *

Marcar apenas uma oval.

- ◯ Muito pouco
- ◯ Pouco
- ◯ Nada
- ◯ Muito
- ◯ Totalmente

35. Você tem medo que sua renda possa ser afetada durante e após esta pandemia? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

36. Você apresentou ou apresenta sintomas típicos da doença COVID-19 (tosse, falta de ar, febre e/ou perda de olfato? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

37. Você recebeu o diagnóstico confirmado de COVID-19? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

38. Você tem medo de contrair a COVID-19? *

Marcar apenas uma oval.

- ◯ Muito pouco
- ◯ Pouco
- ◯ Nada
- ◯ Muito
- ◯ Totalmente

39. Você tem medo de morrer de COVID-19? *

Marcar apenas uma oval.

- ◯ Muito pouco
- ◯ Pouco
- ◯ Nada
- ◯ Muito
- ◯ Totalmente

40. Você tem medo de que a COVID-19 possa piorar o seu quadro da Esclerose Múltipla? *

Marcar apenas uma oval.

- ◯ Muito pouco
- ◯ Pouco
- ◯ Nada
- ◯ Muito
- ◯ Totalmente

41. Você apresentou algum surto da esclerose múltipla nos últimos dois meses? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

42. Você se vacinou para gripe (influenza)? *

Marcar apenas uma oval.

- ◯ Sim
- ◯ Não

Nas últimas 2 semanas, com que frequência você tem sido incomodado(a) pelos seguintes problemas?

43. Nervoso, ansioso, no limite *

Marcar apenas uma oval.

- ◯ Nenhuma vez
- ◯ Alguns dias
- ◯ Mais da metade dos dias
- ◯ Quase todo dia

44. Não ser capaz de parar ou controlar as preocupações *

Marcar apenas uma oval.

- ◯ Nenhuma vez
- ◯ Alguns dias
- ◯ Mais da metade dos dias
- ◯ Quase todo dia

45. Preocupação excessiva sobre diversas coisas *

Marcar apenas uma oval.

- ◯ Nenhuma vez
- ◯ Alguns dias
- ◯ Mais da metade dos dias
- ◯ Quase todo dia

46. Dificuldade de relaxar *

Marcar apenas uma oval.

- ◯ Nenhuma vez
- ◯ Alguns dias
- ◯ Mais da metade dos dias
- ◯ Quase todo dia

47. Tão agitado que não consegue sentar quieto *

Marcar apenas uma oval.

- ◯ Nenhuma vez
- ◯ Alguns dias
- ◯ Mais da metade dos dias
- ◯ Quase todo dia

48. Facilmente irritado ou incomodado *

Marcar apenas uma oval.

- ◯ Nenhuma vez
- ◯ Alguns dias
- ◯ Mais da metade dos dias
- ◯ Quase todo dia

49. Medo que algo terrivel possa acontecer *

Marcar apenas uma oval.

- ◯ Nenhuma vez
- ◯ Alguns dias
- ◯ Mais da metade dos dias
- ◯ Quase todo dia

ANEXO 4 – QUESTIONÁRIO GAD 7

Nas últimas 2 semanas, com que frequência você tem sido incomodado pelos dos dias dia seguintes problemas?	Nenhuma (0)	Vários dias (1)	Mais da metade dos dias (2)	Quase todo dia (3)
Nervoso, ansioso, no limite				
Não ser capaz de parar ou controlar as preocupações				
Preocupação excessiva sobre diversas coisas				
Dificuldade de relaxar				
Tão agitado que não consegue sentar quieto				
Facilmente irritado ou incomodado				
Medo que algo terrível possa acontecer				

ANEXO 5 – Normas para submissão na revista *Multiple Sclerosis Journal*

Manuscript Submission Guidelines:

Manuscript Submission Guidelines: *Multiple Sclerosis Journal*

This Journal is a member of the Committee on Publication Ethics.

This Journal recommends that authors follow the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals formulated by the International Committee of Medical Journal Editors (ICMJE).

Please read the guidelines below then visit the Journal's submission site http://mc.manuscriptcentral.com/multiple-sclerosis to upload your manuscript. Please note that manuscripts not conforming to these guidelines may be returned.

Only manuscripts of sufficient quality that meet the aims and scope of *Multiple Sclerosis Journal* will be reviewed.

There are no fees payable to submit or publish in this journal.

As part of the submission process you will be required to warrant that you are submitting your original work, that you have the rights in the work, and that you have obtained and can supply all necessary permissions for the reproduction of any copyright works not owned by you, that you are submitting the work for first publication in the Journal and that it is not being considered for publication elsewhere and has not already been published elsewhere. Please see our guidelines on prior publication and note that *Multiple Sclerosis Journal* may accept submissions of papers that have been posted on pre-print servers; please alert the Editorial Office when submitting (contact details are at the end of these guidelines) and include the DOI for the preprint in the designated field in the manuscript submission system. Authors should not post an updated version of their paper on the preprint server while it is being peer reviewed for possible publication in the journal. If the article is accepted for publication, the author may re-use their work according to the journal's author archiving policy.

1. What do we publish?

1.1 Aims & Scope

Before submitting your manuscript to *Multiple Sclerosis Journal*, please ensure you have read the Aims & Scope.

1.2 Article Types

Please read the following carefully and ensure that your submission meets the requirements to avoid automatic return or delay in the consideration of your paper.

All papers submitted to *MSJ* are required to provide an Author Declaration form along side your manuscript files prior to submission. The form must include all co-author signatures.

IMPORTANT: The journal no longer solicits Systematic Reviews.

MSJ is now requiring authors to provide the essential requirements of MRI imaging as supplementary data in order to help replication of studies. If submitting a manuscript using MRI data please use this msj_mri_journal.doc to supply the necessary data in a suitable format.

Original research papers

Original research papers should be no more than 3,000 words and contain the following sections: Title page, Abstract, Introduction, Materials (or patients or animals) and Methods, Results, Discussion, Acknowledgements, References, Tables, Figure legends, Figures (see 'Sections of the manuscript' for further details).

Case Reports, Short Reports

The Editors will consider for rapid publication Case Reports and Short Reports that illustrate important points. These must not exceed 1000 words in length, must have a title page, a short summary of no more than 100 words, up to 10 references, one figure and one table.

Letters to the Editor

Brief letters raising pertinent issues relating to recently published papers in *Multiple Sclerosis Journal* or stand-alone letters on topics of interest are welcome. They will be reviewed and may be sent to the first author of the article being discussed for a possible response. They should be in letter format without an abstract. Stand-alone letters on topics of interest will be reviewed and should be in letter format without an abstract.

Personal Viewpoints

Viewpoints which bring new ideas and stimulate discussion and debate are welcomed by the Editors, in particular those that will be of general interest, and which question or comment on new and significant MS-related studies. These will be reviewed and should be no more than 1,500 words, up to 10 references, one figure and one table (if necessary).

Topical Reviews

Topical Reviews focus on specific subjects of current interest where there have been recent and significant advances, ranging from basic neuroscience to clinical and more 'applied' areas. They are short, factual, focussed updates, comprising: Title page, an Abstract of 100-150 words, 5 or so Keywords, 2,500 words of text (excluding references), a limited number of relevant and recent references (up to 35 or so), and a figure if appropriate. See examples from the journal for more information. Topical Reviews are generally by invitation.

Controversies in Multiple Sclerosis

Controversies focus on current issues, with contrasting contributions from leading experts, and cover topics of debate from basic neuroscience to clinical and more 'applied' areas. They necessarily represent an opinion, but are founded on factual evidence. Each Controversy comprises: i) a proposal for a particular view; ii) a presentation of a contrasting view; and iii) an overview/summary. The two opposing views comprise no more than 1,000 words each, supported by no more than 10 key references. The summary piece is based on the opposing statements, and is about 500 words in length. See examples from the journal for more information. We welcome ideas for topics and potential authors, if you have an appropriate idea for

a topic and authors to write a Proposal or Rebuttal, please contact the Controversies editors via the editorial office to discuss further: msjjournal@sagepub.co.uk.

Editorials

Editorials may be solicited by the Editors to address particular topics relating to one or more papers in a given issue.

Insights into

Insights into… is a series of short pieces that provide clear, concise and straightforward information into areas that many of us find challenging. They must be no more than 500 words a piece and provided in a collection of related pieces on the same topic (4-6). They should have a title page, a short summary of no more than 100 words (optional), up to 10 references, one figure and one table.

Future Perspectives

Future Perspectives can provide a forum to help capture the work of groups established to improve or update areas of fundamental importance to MS such as clinical and imaging outcomes. Articles will be reviewed and ideally should be no more than 1,500 words, up to 10 references, one figure and one table (if required).

Book and Meeting Reviews

These reviews are solicited by the Editors.

Note*:* While Editorials, Reviews (including book and meeting reviews), and Topical Reviews will usually be solicited by the Editors, suggestions for topics or brief outlines of proposals are very welcome and can be sent to the nearest regional Editor.

Data previously published in un-reviewed format

The Editors will also consider for publication manuscripts containing data already in press elsewhere or published previously in un-reviewed format, such as abstracts or camera-ready papers for proceedings of scientific meetings. The new manuscript should differ from the one previously published and should not contain any identical

tables or figures. It will be the responsibility of the senior author to bring to the Editor's attention details of previous publications and if necessary, attach relevant documents for the use of referees. The existence of such related paper(s) (published or in press) should be mentioned as a footnote to the manuscript or documented with appropriate references. The Editorial decision will take account of the originality of the work submitted for publication and the extent to which readers of *Multiple Sclerosis Journal* may be expected to have access to the book or journal in which the associated papers have appeared.

Related papers

Related papers either published or in press may be sent with the manuscript for the attention of the Editor.

Short reports on null or negative results

The journal considers the results of rigorous, well-designed studies that demonstrate "no effect" or that fail to replicate previous work ("negative data") as important to the advancement of science. *MSJ* welcomes short reports on null or negative results as long as the papers are based on strong hypothesis testing.

Table 1: Overview of the requirements for manuscript submissions for *MSJ*:

Article type	Abstract	Main text word limit*	References**	Figures/Tables
Original Research Paper	200	3,000	Up to 35	As necessary
Topical Review	100-150	2,500	Up to 35	As necessary
Controversies in Multiple Sclerosis (invitation)	N/A	1,000	5-10	As necessary
Case Report/ Short Reports	100	1,000	10	1-2
Insights into (invitation)	100	500 per piece	10	1
Letter to the Editor	N/A	500	3-5	N/A
Personal Viewpoints/Future Perspective	N/A	1,500	10	1
Invited Editorial	N/A	1000	10	N/A

*Excludes references, tables and legends
**For reference style please see section 4.4

1.3 Writing your paper

The SAGE Author Gateway has some general advice and on how to get published, plus links to further resources.

1.3.1 Make your article discoverable

When writing up your paper, think about how you can make it discoverable. The title, keywords and abstract are key to ensuring readers find your article through search engines such as Google. For information and guidance on how best to title your article, write your abstract and select your keywords, have a look at this page on the Gateway: How to Help Readers Find Your Article Online.

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2. Editorial policies

2.1 Peer review policy

Multiple Sclerosis Journal operates a conventional single-blind reviewing policy in which the reviewer's name is always concealed from the submitting author.

Papers will be sent for anonymous review by at least two reviewers who will either be members of the Editorial Board or others of similar standing in the field. In order to shorten the review process and respond quickly to authors the Editors may triage a submission and come to a decision without sending the paper for external review.

The Editors' decision is final and no correspondence can be entered into concerning manuscripts considered unsuitable for publication in *Multiple Sclerosis Journal*. All correspondence, including notification of the Editors' decision and requests for revisions, will be sent by email.

2.2 Authorship

Papers should only be submitted for consideration once consent is given by all contributing authors. Those submitting papers should carefully check that all those whose work contributed to the paper are acknowledged as contributing authors.

The list of authors should include all those who can legitimately claim authorship. This is all those who:

1. Made a substantial contribution to the concept or design of the work; or acquisition, analysis or interpretation of data,
2. Drafted the article or revised it critically for important intellectual content,
3. Approved the version to be published,
4. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

Authors should meet the conditions of all of the points above. When a large, multicentre group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship.

Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship, although all contributors who do not meet the criteria for authorship should be listed in the Acknowledgments section. Please refer to the International Committee of Medical Journal Editors (ICMJE) authorship guidelines for more information on authorship.

2.3 Acknowledgements

All contributors who do not meet the criteria for authorship should be listed in an Acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, or a department chair who provided only general support.

2.3.1 Third party submissions

Where an individual who is not listed as an author submits a manuscript on behalf of the author(s), a statement must be included in the Acknowledgements section of the manuscript and in the accompanying cover letter. The statements must:

- Disclose this type of editorial assistance – including the individual's name, company and level of input
- Identify any entities that paid for this assistance
- Confirm that the listed authors have authorized the submission of their manuscript via third party and approved any statements or declarations, e.g. conflicting interests, funding, etc.

Where appropriate, SAGE reserves the right to deny consideration to manuscripts submitted by a third party rather than by the authors themselves.

2.3.2 Writing assistance

Individuals who provided writing assistance, e.g. from a specialist communications company, do not qualify as authors and so should be included in the Acknowledgements section. Authors must disclose any writing assistance – including the individual's name, company and level of input – and identify the entity that paid for this assistance").

It is not necessary to disclose use of language polishing services.

Any acknowledgements should appear first at the end of your article prior to your Declaration of Conflicting Interests (if applicable), any notes and your References.

2.4 Funding

Multiple Sclerosis Journal requires all authors to acknowledge their funding in a consistent fashion under a separate heading. Please visit the Funding Acknowledgements page on the SAGE Journal Author Gateway to confirm the format of the acknowledgment text in the event of funding, or state that: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

2.5 Declaration of conflicting interests

It is the policy of *Multiple Sclerosis Journal* to require a declaration of conflicting interests from all authors enabling a statement to be carried within the paginated pages of all published articles.

Please ensure that a 'Declaration of Conflicting Interests' statement is included at the end of your manuscript, after any acknowledgements and prior to the references. If no conflict exists, please state that 'The Author(s) declare(s) that there is no conflict of interest'. For guidance on conflict of interest statements, please see the ICMJE recommendations here.

2.6 Research ethics and patient consent

Medical research involving human subjects must be conducted according to the World Medical Association Declaration of Helsinki.

Submitted manuscripts should conform to the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals, and all papers reporting animal and/or human studies must state in the methods section that the relevant Ethics Committee or Institutional Review Board provided (or waived) approval. Please ensure that you have provided the full name and institution of the review committee, in addition to the approval number.

For research articles, authors are also required to state in the methods section whether participants provided informed consent and whether the consent was written or verbal.

Information on informed consent to report individual cases or case series should be included in the manuscript text. A statement is required regarding whether written informed consent for patient information and images to be published was provided by the patient(s) or a legally authorized representative. Please do not submit the patient's actual written informed consent with your article, as this in itself breaches the patient's confidentiality. The Journal requests that you confirm to us, in writing, that you have obtained written informed consent but the written consent itself should be held by the authors/investigators themselves, for example in a patient's hospital record. The confirmatory letter may be uploaded with your submission as a separate file.

Please also refer to the ICMJE Recommendations for the Protection of Research Participants.

All research involving animals submitted for publication must be approved by an ethics committee with oversight of the facility in which the studies were conducted. The journal has adopted the Consensus Author Guidelines on Animal Ethics and Welfare for Veterinary Journals published by the International Association of Veterinary Editors.

2.7 Clinical trials

Multiple Sclerosis Journal conforms to the ICMJE requirement that clinical trials are registered in a WHO-approved public trials registry at or before the time of first patient enrolment as a condition of consideration for publication. The trial registry name and URL, and registration number must be included at the end of the abstract.

2.8 Reporting guidelines

The relevant EQUATOR Network reporting guidelines should be followed depending on the type of study. For example, all randomized controlled trials submitted for publication should include a completed CONSORT flow chart as a cited figure and the completed CONSORT checklist should be uploaded with your submission as a supplementary file. Systematic reviews and meta-analyses should include the completed PRISMA flow chart as a cited figure and the completed PRISMA checklist should be uploaded with your submission as a supplementary file. The EQUATOR wizard can help you identify the appropriate guideline.

Other resources can be found at NLM's Research Reporting Guidelines and Initiatives.

2.9 Research Data

The journal is committed to facilitating openness, transparency and reproducibility of research, and has the following research data sharing policy. For more information, including FAQs please visit the SAGE Research Data policy pages.

Subject to appropriate ethical and legal considerations, authors are encouraged to:

- share your research data in a relevant public data repository

- include a data availability statement linking to your data. If it is not possible to share your data, we encourage you to consider using the statement to explain why it cannot be shared.
- cite this data in your research

Multiple Sclerosis Journal requests all authors submitting any primary data used in their research articles alongside their article submissions to be published in the online version of the journal, or provide detailed information in their articles on how the data can be obtained. This information should include links to third-party data repositories or detailed contact information for third-party data sources. Data available only on an author-maintained website will need to be loaded onto either the journal's platform or a third-party platform to ensure continuing accessibility. Examples of data types include but are not limited to statistical data files, replication code, text files, audio files, images, videos, appendices, and additional charts and graphs necessary to understand the original research. The editor may consider limited embargoes on proprietary data. The editor can also grant exceptions for data that cannot legally or ethically be released. All data submitted should comply with Institutional or Ethical Review Board requirements and applicable government regulations.thors should also follow data citation principles. For more information please visit the SAGE Author Gateway, which includes information about SAGE's partnership with the data repository Figshare.

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3. Publishing Policies

3.1 Publication ethics

SAGE is committed to upholding the integrity of the academic record. We encourage authors to refer to the Committee on Publication Ethics' International Standards for Authors and view the Publication Ethics page on the SAGE Author Gateway.

3.1.1 Plagiarism

Multiple Sclerosis Journal and SAGE take issues of copyright infringement, plagiarism or other breaches of best practice in publication very seriously. We seek to protect the rights of our authors and we always investigate claims of plagiarism or

misuse of published articles. Equally, we seek to protect the reputation of the journal against malpractice. Submitted articles may be checked with duplication-checking software. Where an article, for example, is found to have plagiarised other work or included third-party copyright material without permission or with insufficient acknowledgement, or where the authorship of the article is contested, we reserve the right to take action including, but not limited to: publishing an erratum or corrigendum (correction); retracting the article; taking up the matter with the head of department or dean of the author's institution and/or relevant academic bodies or societies; or taking appropriate legal action.

3.1.2 Prior publication

If material has been previously published it is not generally acceptable for publication in a SAGE journal. However, there are certain circumstances where previously published material can be considered for publication. Please refer to the guidance on the SAGE Author Gateway or if in doubt, contact the Editor at the address given below.

3.2 Contributor's publishing agreement

Before publication, SAGE requires the author as the rights holder to sign a Journal Contributor's Publishing Agreement. SAGE's Journal Contributor's Publishing Agreement is an exclusive licence agreement which means that the author retains copyright in the work but grants SAGE the sole and exclusive right and licence to publish for the full legal term of copyright. Exceptions may exist where an assignment of copyright is required or preferred by a proprietor other than SAGE. In this case copyright in the work will be assigned from the author to the society. For more information please visit the SAGE Author Gateway.

3.3 Open access and author archiving

Multiple Sclerosis Journal offers optional open access publishing via the SAGE Choice programme. For more information on Open Access publishing options at SAGE please visit SAGE Open Access. For information on funding body compliance, and depositing your article in repositories, please visit SAGE's Author Archiving and Re-Use Guidelines and Publishing Policies.

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4. Preparing your manuscript for submission

4.1 Formatting

The preferred format for your manuscript is Word. LaTeX files are also accepted. Word and (La)Tex templates are available on the Manuscript Submission Guidelines page of our Author Gateway.

Manuscript Preparation: Submitting a new manuscript through the online system:

When making a submission, the following *separate, unpaginated* documents should be uploaded. Please do not submit one combined document. The separate files will be combined into a pdf in the online system.

1. Title page (title, names of authors, affiliations, keywords, corresponding author)
2. Main document (includes structured abstract, main text, acknowledgements, references)
3. Tables (each as a *separate* Word document)
4. Figure legends (Word document)
5. Figures (as *separate* tiff, jpg or eps files)
6. Any supplementary files

Submitting a Revision:

After review the editors may invite submission of a revised manuscript. When submitting a revision, delete the original files (as these are saved with your original submission), and upload your revised manuscript only, following the usual submission guidelines. Changes to the manuscript must be marked using highlighting or track changes, and the authors' response to the reviewers' comments should be placed in appropriate box during the submission process. The text should be double-spaced throughout and with a minimum of 3cm for left and right hand margins and 5cm at head and foot. Text should be standard 10 or 12 point. Word counts as outlined in Table 1 re initial submissions, should still be adhered to.

Title page

The title should be concise with no abbreviations. Please provide the surname, initials, department, institution, city and country of each author, and the name, email address, full mailing address, telephone number and fax number of the corresponding author to whom proofs should be sent. List six to eight keywords (chosen from Index Medicus, Medical Subject Headings if possible).

Abstract

The second page of the manuscript must contain only the abstract, which should be of no more then 200 words and must be clearly written and comprehensive to readers before they have to read the paper.
The abstract should be structured according to the following sub headings: Background, Objective, Methods, Results and Conclusion. Abbreviations should be avoided and reference citations are not permitted.
Any manuscripts submitted without a structured abstract will be returned to the author immediately without peer review, thus delaying the evaluation process of the manuscript.

Introduction

The introduction should assume that the reader is knowledgeable in the field and be as brief as possible.

Materials and Methods

Methods that have been published in detail elsewhere should not be described in detail. Avoid unnecessary detailed descriptions of widely used techniques. SI Units should be used throughout the text. Reports of experiments involving patients and healthy volunteers must describe the steps taken to obtain consent and to maintain confidentiality. Experiments involving animals must conform to accepted ethical standards.

Tables

Tables should be submitted in Word, typed on separate pages. Tables should be numbered consecutively with Arabic numerals, and cited as such in the manuscript.

The preferred placing of tables in the main text should be indicated. Tables should include a brief descriptive title and be self-explanatory. Footnotes to tables indicated by lower-case superscript letters are acceptable, but they should not include extensive experimental details.

4.1.1 Units, Symbols and abbreviation

For detailed advice please refer to the guidelines in Baron, DN (1988). Units, symbols and abbreviations, 4th edn. (Obtainable from The Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE, UK).

Note that the SI system of units is preferred. Due to the multidisciplinary nature of the readership and to avoid confusion, the number of abbreviations in the text should be kept to a minimum. Standard abbreviations acceptable without definition are limited to the following:

- CNS (central nervous system); CSF (cerebrospinal fluid); DNA (deoxyribonucleic acid); HLA (human leukocyte antigen; MRI (magnetic resonance imaging); CT (computerized tomography); MS (multiple sclerosis); RNA (ribonucleic acid).

Nonstandard definitions must be defined in full at their first usage in the abstract and again at their first use in the text.

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