

Dietary habits in a group of patients with multiple sclerosis are similar to those of healthy control subjects

Hábitos alimentares de pacientes com esclerose múltipla são semelhantes àqueles de controles saudáveis

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ABSTRACT

Background: Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system. Over time, patients with MS accumulate neurological disabilities. MS typically affects young adults and is associated with an inflammatory profile of cytokines and lymphocytes. If a patient were to consume a potentially inflammatory diet, it is possible that the evolution of MS in that individual would be more aggressive. **Objective:** To investigate whether patients with MS living in and around the city of Santos, São Paulo, Brazil, had a profile of inflammatory diet. **Methods:** Patients with MS and healthy control subjects were individually interviewed, and the 24-hour Diet Recall and the Bristol Stool Form Scale were applied. Salt intake was calculated using the WebDiet 2.0 software. **Results:** There were no remarkable differences in dietary habits between healthy control subjects (n=34) and patients with MS (n=66), except for higher consumption of carbohydrates by patients. Both patients with MS and control subjects had higher protein and lower carbohydrate intake than the World Health Organization's recommended daily amounts. There was no correlation between food intake and neurological disability in patients with MS. **Conclusion:** The dietary patterns of patients with MS and healthy controls were similar in the city of Santos, São Paulo, Brazil, and surrounding towns, except for higher intake of carbohydrates by patients. No profile of pro-inflammatory diets was identified among the patients with MS enrolled in this study.

Keywords: Multiple Sclerosis; Diet; Nutritional Sciences; Inflammation; Neurology.

RESUMO







Introdução: Esclerose múltipla (EM) é uma doença crônica e autoimune do sistema nervoso central. Ao longo do tempo, pacientes com EM acumulam incapacidades neurológicas. A EM tipicamente afeta adultos jovens e se associa a um perfil inflamatório de citocinas e linfócitos. Se um paciente tiver uma dieta potencialmente inflamatória, é possível que a evolução da EM seja mais agressiva neste indivíduo. **Objetivo:** Investigar se pacientes com EM residentes na cidade de Santos e região, São Paulo, Brasil, apresentam um perfil de dieta inflamatória. **Métodos:** Pacientes com EM e controles saudáveis foram individualmente entrevistados e um Recordatório da Dieta de 24 horas e a Escala de Bristol de Tipo de Fezes foram aplicadas. A ingestão de sal foi calculada usando o WebDiet 2.0 *software*. **Resultados:** Não houve diferença marcante nos hábitos alimentares de controles saudáveis (n=34) e pacientes com EM (n=66), exceto pelo maior consumo de carboidratos pelos pacientes. Tanto os pacientes com esclerose múltipla quanto controles tinham maior consumo de proteína e menor consumo de carboidratos do que o recomendado pela Organização Mundial de Saúde. Não houve correlação entre o consumo de alimentos e a incapacidade neurológica dos pacientes com EM. **Conclusão:** O padrão de dieta de pacientes com EM e controles saudáveis é semelhante na cidade de Santos, SP, Brasil e região circunvizinha, exceto pelo maior consumo de carboidratos pelos pacientes. Não foi identificado um perfil de dieta pró-inflamatória entre os pacientes incluídos neste estudo.

Palavras-chave: Esclerose Múltipla; Dieta; Ciências da Nutrição; Inflamação; Neurologia.

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INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS) that mainly affects young adults¹. Although MS is a relatively rare disease, there are circa 2.3 million individuals with MS worldwide^{2,3}. The cause of MS is unknown, but pathological findings include inflammation and degeneration of the CNS⁴. Briefly, MS is likely to be the result of a combination of genetic predisposition and environmental influences⁵. MS is an important cause of neurological disability, unemployment and low quality of life among young and middle-aged adults⁶. This devastating disease can be treated with disease-modifying therapies, which have evolved with remarkable speed⁷. At present, most patients with an early diagnosis of MS can expect good disease control and less neurological disability when followed by experienced neurologists. However, as patients get older, age-related diseases may start to superimpose disabilities on those who already have chronic neurological conditions. For example, metabolic and cardio/cerebrovascular diseases may lead to stroke in a patient with MS⁸.

Healthy lifestyle interventions may decrease inflammation and are important tools during the patients' treatment. Physical exercise, for example, is beneficial for patients with MS for a variety of reasons, including through changing their cytokine profile to an anti-inflammatory pattern^{9,10,11}. Likewise, patients with MS should improve their diet, so as to avoid components associated with an inflammatory profile. The long-chain fatty acids that are often found in processed foods promote differentiation of naïve T cells into pro-inflammatory Th1 and Th17 cells¹². On the other hand, polyunsaturated fatty acids (PUFA) decrease inflammation through expression of anti-inflammatory prostaglandins E1 and E2, which will affect cytokine production and leukocyte migration¹³.

Regarding salt, while some authors have reported that high salt intake was associated with an inflammatory Th17 cell profile and worse outcomes among patients with MS^{14,15}, others have not shown such results¹⁶.

Higher intake of fruits and vegetables has been correlated with reduced levels of MS disease activity, symptom burden, and neurological disability in large studies¹⁷. An inverse relationship between whole-grain intake and MS-related disability has been described¹⁸.

The objective of the present study was to compare the dietary patterns of patients with MS and healthy control subjects living along the seacoast, in and around the city of Santos, São Paulo, Brazil.

METHODS

The study was approved by the Ethics Committee at Universidade Metropolitana de Santos (UNIMES), São Paulo, Brazil. All the subjects with MS were living in the city of Santos (23°57'38.99" S; 46°20'1" W) and surrounding towns

and were receiving medical care from specialized neurologists at the University Reference Centre for MS, at the MS & Headache Centre Santos, and at private consultation offices. Patients were recruited from the two associations for MS in Santos, namely Associação de Portadores de Esclerose Múltipla da Baixada Santista (APEMBS) and Esclerose Múltipla Litoral Santista (ALSAPEM). Control subjects were healthy individuals accompanying friends of family to consultations at several medical services at UNIMES). Participation was voluntary and only those who signed the informed consent were included.

In order to avoid biases associated with sedentarism and motor limitations, only patients who could walk for at least 100 m with or without a cane were included. The patients' neurological disability was measured using the Expanded Disability Scale Score (EDSS), which can range from zero (normal neurological examination) to 10 (death) in increments of 0.5 points¹⁹. All the patients in this study presented EDSS≤6.0, meaning they were not wheelchair-bound or bedridden.

Briefly, patients and controls were included if they volunteered to participate, signed the informed consent and were able to understand the questions and interact with the interviewers. Patients were excluded if they were wheelchair-bound or bedridden. Participants informed their height and weight.

Dietary intake was assessed during a personal interview using a 24-hour recall questionnaire. Intake measurements were estimated using simple drawings of plates, cutlery, glasses, etc. This method enabled the assessment of macronutrients, carbohydrates, proteins, and fat. The standard diet established by the World Health Organization (WHO) includes 60% carbohydrates, 25% fat, and 15% protein²⁰. These percentages were used as ideal values in our study. The interviewers had been extensively trained for this project. Salt intake was calculated using the WebDiet 2.0 software.

The Bristol Stool Form Scale²¹, as validated for use in Brazilian Portuguese²², was used to assess the characteristics of the patients' feces. Seven drawings of different types of stool were shown to the patients, who selected their predominant type on the basis of shape and consistency.

The statistical analyses used included sample size calculation (minimum n=28 in each group), the Shapiro-Wilk test for normality, Student's *t*-test for parametric comparison between groups and Pearson's correlation test; p<0.05 was used to define statistically significant differences.

RESULTS

The group consisted of 66 patients with MS (13 men; 19.9%) and 34 healthy control volunteers (nine men, 26%). At least 12 months had elapsed since MS onset in these patients. The mean age of the two groups was not statistically different. Patients with MS had had a median disease duration of seven years and presented median EDSS of 2.0 (minimal disability). Table 1 summarizes the results from this study.

Table 1. Comparative data between patients with multiple sclerosis and healthy controls. Results are presented as mean value±standard deviation.

	MS (n=66)	Control (n=34)	p-value Control × MS
MS duration (years)	7.8±3.7		
EDSS	2.1±1.4		
Male / female	13 / 53	9 / 25	0.45
Age (years)	41.2±11.7	39.7±13.7	0.60
BMI	25.4±4.65	25.9±3.95	0.93
PTN (g)	104.5±28.8	105.6±54.6	0.89
LIP (g)	55.5±28.8	53.1±31.6	0.69
CHO (g)	230.7±93.1	187.9±77.4	0.02*
Kcal	1,841.2±609.1	1,652.0±672.7	0.15
% PTN	23±9	26±10	0.21
% LIP	27±8	28±8	0.39
% CHO	50±11	45±11	0.09
Feces times/week	5.8±2.4	6.2±3.1	0.46
Bristol scale	3.2±0.9	3.1±0.9	0.76

*Significant difference in the intake of carbohydrates; MS: multiple sclerosis; EDSS: Expanded Disability Scale Score [Kurtzke]; BMI: body mass index; g: grams; PTN: protein; LIP: lipids; CHO: carbohydrates; Kcal: kilocalories/day.

Patients with MS consumed higher levels of carbohydrates than control subjects ($p=0.02$). There was no correlation between patients' disability and intake of kilocalories, carbohydrates, protein or fat ($r\leq 0.1$ for all calculations). In comparison with the WHO recommendations, these patients with MS and control subjects living in the coastal area of southeastern Brazil had higher protein and lower carbohydrate intake levels in their diets. The daily intake of salt and fibers was within the levels recommended by the WHO for both groups. Patients ingested 1,484 mg of salt and 21.4 g of fiber/day, while controls ingested 1,136 mg of salt and 18g of fiber/day. The WHO recommended values are 1,500 mg of salt and 25 g of fiber/day. The water intake levels among the patients and controls were 1.340 L/day and 1.470 L/day, respectively, *i.e.* lower than the 2 liters/day recommended by the WHO. This finding is consistent with the low hydration of these individuals' feces, since 14.7% of the controls and 19.6% of the patients reported having hard stools. However, there was no correlation between water intake and hardened feces in this sample.

DISCUSSION

There are few case-control studies on the dietary habits of patients suffering from MS. Epidemiological data suggest that a pro-inflammatory diet increases the risk of developing MS^{23,24}, while fish oils²⁵ and a Mediterranean diet²⁶ could protect individuals from having the disease. The present study neither found any correlation between dietary habits and neurological

disability, nor any significant difference between food intake by patients with MS and controls. The patients with MS in the present study were regularly attended by a neurologist specializing in this disease. Therefore, it is possible that through having low disability, attending discussions at the patients' associations and having proper medical care, these patients already had better lifestyle leading to an "anti-inflammatory behavior". This hypothesis is reinforced by a recent study from Spain, in which patients with severe degrees of MS disability were often malnourished or at risk of malnutrition, with deficient intake of polyunsaturated fatty acids, fibers, and vitamins²⁷. Another study showed that disability among patients with MS measured through EDSS correlated with the "Dietary Inflammatory Index"²⁸.

Living along the seacoast, just south of the Tropic of Capricorn, is possibly another favorable factor. The population enrolled in this study is exposed to sunlight and tends to use light clothing. There are free physical activity programs on the beach and in gyms, and most people in Santos and surrounding towns have a culture of "staying fit", as observed from the body mass index (BMI) of the individuals enrolled in this study. With a median age of 40 years, the median BMI was 25.5 among the 100 participants in this study. Furthermore, the pattern of higher protein intake and lower carbohydrate intake reinforces the idea that these individuals were practicing weight control. The low daily caloric intake seems to reinforce this hypothesis. Although patients with MS consumed more carbohydrates than control subjects, the values for both groups were below those recommended by the WHO.

The feces from all the individuals enrolled in this study were within the normal range on the validated scale containing seven types of stool forms. All participants reported having forms 2, 3 or 4 (normal). Water intake and feces consistency were not correlated, but the very narrow variation of both parameters must be taken into consideration.

This study has some limitations. A 24-hour recall questionnaire is a valuable tool but there may be a tendency to overestimate low food intakes and underestimate high ones²⁹. Well-trained interviewers can overcome most difficulties with the method through using a detailed and thorough procedure protocol³⁰. The population of this study was relatively small and was restricted to a relatively small area of residence. Therefore, the results may not be applicable to different parts of the world. In addition, the inclusion of patients with MS with low or moderate disability means that the more severe cases of MS were excluded from the study. Thus, the results obtained in this study may not be reproducible for all patients with MS in the 23°57'38.99" S, 46°20'1" W region.

In conclusion, except for higher intake of carbohydrates among the patients, the dietary patterns of patients with MS and healthy controls in the city of Santos, São Paulo, Brazil, and surrounding towns were similar. No profile of pro-inflammatory diets was observed among the patients with MS enrolled in this study. The patients and control subjects consumed more protein and less carbohydrates than recommended by the WHO.

References

1. Yamout BI, Alroughani R. Multiple sclerosis. *Semin Neurol*. 2018;38(2):212-25. <https://doi.org/10.1055/s-0038-1649502>
2. Markowitz CE. Multiple sclerosis update. *Am J Manag Care*. 2013 Nov;19(16 Suppl):s294-300.
3. Rosati G. The prevalence of multiple sclerosis in the world: an update. *Neurol Sci*. 2001 Apr;22(2):117-39. <https://doi.org/10.1007/s100720170011>
4. Lassmann H. Multiple sclerosis pathology. *Cold Spring Harb Perspect Med*. 2018;8:a028936. <https://doi.org/10.1101/cshperspect.a028936>
5. Olsson T, Barcellos LF, Alfredsson L. Interactions between genetic, lifestyle and environmental risk factors for multiple sclerosis. *Nat Rev Neurol*. 2017 Mar;13(1):25-36. <https://doi.org/10.1038/nrneurol.2016.187>
6. Wilski M, Gabrylski J, Broła W, Tomasz T. Health-related quality of life in multiple sclerosis: Links to acceptance, coping strategies and disease severity. *Disabil Health J*. 2019 Oct;12(4):608-14. <https://doi.org/10.1016/j.dhjo.2019.06.003>
7. Gholamzad M, Ebtakar M, Ardestani MS, Azimi M, Mahmodi Z, Mousavi MJ, et al. A comprehensive review on the treatment approaches of multiple sclerosis: currently and in the future. *Inflamm Res*. 2019 Jan;68(1):25-38. <https://doi.org/10.1007/s00011-018-1185-0>
8. Thorburn AN, Macia L, Mackay CR. Diet, metabolites, and “western-lifestyle” inflammatory diseases. *Immunity*. 2014;40(6):833-42. <https://doi.org/10.1016/j.immuni.2014.05.014>
9. Motl RW, Sandroff BM, Kwakkel G, Dalgas U, Feinstein A, Heesen C, et al. Exercise in patients with multiple sclerosis. *Lancet Neurol*. 2017 Oct;16(10):848-56. [https://doi.org/10.1016/S1474-4422\(17\)30281-8](https://doi.org/10.1016/S1474-4422(17)30281-8)
10. Donia SA, Allison DJ, Gammage KL, Ditor DS. The effects of acute aerobic exercise on mood and inflammation in individuals with multiple sclerosis and incomplete spinal cord injury. *NeuroRehabilitation*. 2019 Sep;45(1):117-24. <https://doi.org/10.3233/NRE-192773>
11. Barry A, Cronin O, Ryan AM, Sweeney B, O'Toole O, O'Halloran KD, et al. Cycle ergometer training enhances plasma interleukin-10 in multiple sclerosis. *Neurol Sci*. 2019 Apr;40(9):1933-6. <https://doi.org/10.1007/s10072-019-03915-2>
12. Haghikia A, Jörg S, Duscha A, Berg J, Manzel A, Waschbisch A, et al. Dietary fatty acids directly impact central nervous system autoimmunity via the small intestine. *Immunity*. 2015 Oct;43(4):817-29. <https://doi.org/10.1016/j.immuni.2015.09.007>
13. von Geldern G, Mowry EM. The influence of nutritional factors on the prognosis of multiple sclerosis. *Nat Rev Neurol*. 2012 Dec;8(12):678-89. <https://doi.org/10.1038/nrneurol.2012.194>
14. Farez MF, Fiol MP, Gaitan MI, Quintana FJ, Correale J. Sodium intake is associated with increased disease activity in multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2015;86(1):26-31. <https://doi.org/10.1136/jnnp-2014-307928>
15. Kleinewietfeld M, Manzel A, Titze J, Kvakon H, Yosef N, Linker RA, et al. Sodium chloride drives autoimmune disease by the induction of pathogenic TH17 cells. *Nature*. 2013 Mar;496(7446):518-22. <https://doi.org/10.1038/nature11868>
16. Nourbakhsh B, Graves J, Casper TC, Lulu S, Waldman A, Belman A, et al. Dietary salt intake and time to relapse in paediatric multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2016 Dec;87(12):1350-3. <https://doi.org/10.1136/jnnp-2016-313410>
17. Hadgkiss EJ, Jelinek GA, Weiland TJ, Pereira NG, Marck CH, van der Meer DM. The association of diet with quality of life, disability, and relapse rate in an international sample of people with multiple sclerosis. *Nutr Neurosci*. 2015 Apr;18(3):125-36. <https://doi.org/10.1179/1476830514Y.0000000117>
18. Fitzgerald KC, Tyry T, Salter A, Cofield SS, Cutter G, Fox R, et al. Diet quality is associated with disability and symptom severity in multiple sclerosis. *Neurology*. 2018;90(1):e1-e11. <https://doi.org/10.1212/WNL.0000000000004768>
19. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983 Nov;33(11):1444-52.
20. World Health Organization. WHO/FAO release independent Expert Report on diet and chronic disease. Available from: <https://www.who.int/mediacentre/news/releases/2003/pr20/en/>
21. Heaton KW, Radvan J, Cripps H, Mountford RA, Braddon FE, Hughes AO. Defecation frequency and timing, and stool form in the general population: a prospective study. *Gut*. 1992;33(6):818-24. <http://dx.doi.org/10.1136/gut.33.6.818>
22. Jozala DR, Oliveira ISF, Ortolan EVP, Oliveira Junior WE, Comes GT, et al. Brazilian Portuguese translation, cross-cultural adaptation and reproducibility assessment of the modified Bristol Stool Form Scale for children. *J Pediatr (Rio J)*. 2019 May/Jun;95(3):321-7. <https://doi.org/10.1016/j.jpeds.2018.01.006>
23. Shivappa N, Hebert JR, Behrooz M, Rashidkhani B. Dietary inflammatory index and risk of multiple sclerosis in a case-control study from Iran. *Neuroepidemiology*. 2016 Sep;47(1):26-31. <https://doi.org/10.1159/000445874>
24. Abdollahpour I, Sormani MP, Nedjat, S, Mansournia MA, van der Mei I. The role of nutritional factors during adolescence in multiple sclerosis onset: a population-based incident case-control study. *Nutr Neurosci*. 2019;1:1-8. <https://doi.org/10.1080/1028415X.2019.1647689>
25. Bäärnhielm M, Olsson T, Alfredsson L. Fatty fish intake is associated with decreased occurrence of multiple sclerosis. *Mult Scler*. 2014;20(6):726-32. <https://doi.org/10.1177/1352458513509508>
26. Black LJ, Baker K, Ponsonby AL, van der Mei I, Lucas RM, Pereira G, et al. A higher Mediterranean diet score, including unprocessed red meat, is associated with reduced risk of central nervous system demyelination in a case-control study of Australian adults. *J Nutr*. 2019 Aug;149(8):1385-92. <https://doi.org/10.1093/jn/nxz089>
27. Redondo Robles L, Pintor de la Maza B, Tejada García J, García Vieitez JJ, Fernández Gómez MJ, et al. Nutritional profile of multiple sclerosis. *Nutr Hosp*. 2019;36(2):340-9. <https://doi.org/10.20960/nh.2023>
28. Da Costa Silva BY, De Carvalho Sampaio HA, Shivappa N, Hebert JR, da Silva Albuquerque L, Ferreira Carioca AA, et al. Interactions between dietary inflammatory index, nutritional state and multiple sclerosis clinical condition. *Clin Nutr ESPEN*. 2018 Aug;26:35-41. <https://doi.org/10.1016/j.clnesp.2018.04.018>
29. Salvador Castell G, Serra-Majem L, Ribas-Barba L. What and how much do we eat? 24-hour dietary recall method. *Nutr Hosp*. 2015;31(Suppl 3):46-48. <https://doi.org/10.3305/nh.2015.31.sup3.8750>
30. Shim JS, Oh K, Kim HC. Dietary assessment methods in epidemiologic studies. *Epidemiol Health*. 2014;36:e2014009. <https://doi.org/10.4178/epih/e2014009>