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ORIGINAL ARTICLE

Association Of Obesity with Relapsing Remitting Multiple Sclerosis Disability in Zagazig University Hospitals.

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ABSTRACT

Background: Previous studies had linked obesity to the pathogenesis and risk of multiple sclerosis (MS) but little is known about its association with disease course. This study aimed to assess the frequency of obesity in MS patients and its relation to disease disability.

Methods: A cross-section study included 60 patients with clinically definite relapsing remitting multiple sclerosis was selected from the inpatients wards and outpatients clinic of Neurology Department, Zagazig during the period from March 2020 to September 2020. All patients underwent a thorough physical and neurological examination, as well as laboratory and radiographic tests. Obesity was diagnosed if body mass index (BMI) ≥30. The Expanded Disability Status Scale (EDSS) was used to assess disease disability. Patients were divided into 2 groups (obese and non-obese) according to BMI.

Results: Obesity frequency was 43.3% (26 MS patients). Obese MS patients had higher disease duration (6.23 ± 4.65) and more disease disability (EDSS= 4.0 ± 2.21). There was positive correlation between BMI with EDSS, disease duration, number of relapses and total cholesterol. Multiple regression analysis showed that EDSS was independently associated with obesity in MS patients.

Conclusion: There was a high frequency of obesity in MS patients. Disease disability (EDSS) was significantly associated with obesity in MS patients. Obesity screening should be a regular component of MS management.

Keywords: Multiple Sclerosis, Obesity, Disability, EDSS, BMI.

INTRODUCTION

Multiple sclerosis (MS) is a multifactorial autoimmune disease, in which chronic inflammation of the central nervous system (CNS) leads to demyelination and neural cell injury in both white and gray matter. It is the most prevalent non-traumatic cause of CNS complications in young people worldwide [1, 2]. Multiple Sclerosis is considered a complex disease, meaning that it results from the interaction of multiple environmental and lifestyle risk factors with an individual and susceptible genetic background [3].Several epidemiologic studies have connected environmental and lifestyle factors to the incidence of MS. Obesity have followed the same pattern of distribution during the same time period as a result of increasingly sedentary lifestyles and changing dietary trends.The increased prevalence of both autoimmune disorders and obesity has prompted researchers to look for similar underlying processes [4]. The prevalence of overweight and obesity has increased dramatically in the last decade, creating a global epidemic [5].Obesity's link to health-related quality of life and disability development has given it an important role in MS research [6]. The possible link between MS and obesity has become more interesting in recent years since the discovery of the remarkable properties of adipose tissue. Once MS is initiated, obesity can contribute to increased disease severity by negatively influencing disease progress and treatment response. Increasing prevalence of obesity in early life has been associated with increased risk of developing MS during childhood and adolescence [7].

This study was to determine the frequency of obesity in MS patients and its relation to disability measured by Expanded Disability Status Scale (EDSS).

METHODS

This cross section study was carried out during the months of March to September 2020. Sixty patients with clinically definite relapsing remitting multiple sclerosis (RRMS) were recruited from the inpatient wards and outpatient clinics of the Zagazig University Hospitals' Neurology

Department. The study was approved by the Ethical Committee of Faculty of Medicine, Zagazig University and informed written consent was obtained from patients or written assent from a relative. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Some of the cases in our sample were diagnosed according to McDonald (2010) [8], whereas McDonald 2017 diagnosed newly diagnosed patients [9]. All patients were subjected to thorough medical history, which included age, sex, and previous medical history, as well as a complete history of their current illness including the number of relapses, symptoms of the current relapse, and disease duration. A thorough physical and neurological examination is performed. Fasting blood glucose (mg/dl), serum triglyceride (TG) (mg/dl), total cholesterol (mg/dl), high density lipoprotein (HDL) (mg/dl), and low density lipoprotein (LDL) (mg/dl) were performed for all patients. Magnetic resonance imaging (MRI) of brain and spinal cord were done using 1.5 Tesla superconducting MR imager (Achieva, Philips Medical System). MRI activity was considered if there are new T2 lesions and/or Gd-enhancing lesion in 2 or more areas of CNS: periventricular, cortical, Juxtacortical, Infratentorial or spinal cord. Assessment of illness disability was done using the Expanded Disability Status Scale (EDSS) [10], a reliable, validated and highly accepted clinical measure. The Expanded Disability Status Scale (EDSS) is the most regularly used rating scale to evaluate the disability of individuals with MS. The patients were assessed on a scale that quantifies dysfunction in eight function systems: pyramidal, cerebellar, brain stem, sensory, visual, bowel and bladder, and other functions. The EDSS score ranges from 0 to 10, with the lowest score indicating normal neurological examination and the highest score suggesting death from MS.

All patients were analyzed for the frequency of obesity. Obesity was measured and defined using body mass index (BMI) [BMI (Kg/m^2) =Weight (Kg) ÷height^2 (m^2)]. Obesity is classified according to body mass index (BMI) as follow: BMI score range of 18.5–24.9 is normal, 25–29.9 is overweight and BMI ≥ 30 is obese [11]. MS patients were divided into 2 groups (obese and non-obese) according to BMI.

STATISTICAL ANALYSIS

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 15 for Windows® (SPSS Inc, Chicago, IL, USA). Qualitative data was presented as number and percent. Comparison between groups was done by Chi-Square test. Quantitative data was tested for normality by Kolmogrov-Smirnov test. Normally distributed data was presented as mean±SD. Pearson's correlation was performed to examine the association between BMI and other variables. Multivariable logistic regression analysis was performed to identify significant factors associated with obesity. Strength of association were expressed as odds ratio (OR) and 95% confidence interval (CI). P-value ≤0.05 was considered significant.

RESULTS

Sixty patients were included in the present study, there were 19 (31.7%) males and 41 (68.3%) females with female to male ratio were 2.16:1. Their ages ranged from 19-55 years and mean age (±SD) was 31.40 (± 8.41). Multiple sclerosis onset occurred at an average age of 27.05 ± 8.01years with a mean disease duration of 4.35 ± 3.89 years.According to the clinical presentation of our MS patients, we found that the most frequent symptoms were pyramidal manifestation (53.3 %) followed by sensory manifestation (18.3 %), cerebellar manifestation (15 %), visual manifestation (13.3 %), bowel and Bladder manifestation (5 %), brain stem manifestation(3.3 %) and neuropsychological manifestation (3.3 %).Regarding the total number of relapses since the onset of the disease, it ranged from 2 to 7 relapses; 20 (33.3%) patients had 2 relapses, 13 (21.7%) patients had 3 relapses, 14 (23.3%) patients had 4 relapses, 9 (15%) patients had5 relapses, 3(5%) patients had 6 relapses and one patient (1.7%) had 7 relapses. Our patients' mean EDSS score was 2.81 (±1.9). Frequency of obesity among the studied MS patients was 43.3% (26 patients) (Table 1). Analysis of the clinical data of the MS patients in this study showed that there was a statistically significant difference between MS patients who were obese and those who were not obese, as regarding BMI, disease duration, total cholesterol and disease disability (EDSS). However, there were no significant differences between both groups as regard age, gender, age of disease onset, number of relapses, fasting blood sugar, TG, LDL, HDL and MRI activity (Table 2). There was positive correlation between BMI with disease duration, disease disability (EDSS), total cholesterol, fasting blood sugar and number of relapses (Table 3). Further analysis with multiple regression analysis of significant variables in univariable analysis demonstrated that EDSS of MS patients was an independent predictor of obesity (Table 4).

Table (1) Demographic characteristics of multiple sclerosis patients**:**

Characteristics	MS patients (N=60)
Sex: N (%)	
Male	**19 (31.7%)**
Female	**41 (68.3%)**
Age (years): Mean±SD	**31.40±8.41**
Age of disease onset (years):	**27.05±8.01**
Disease duration (years): Mean±SD	**4.35± 3.89**
Number of relapse: Mean±SD	**3.42±1.32**
BMI: Mean±SD	**30.25±6.64**
Obesity: N (%)	**26(43.3%)**
EDSS: Mean±SD	**2.81 (±1.9)**

N: number; SD: stander deviation; BMI: Body mass index; EDSS: Expanded Disability Status Scale

Table (2) Comparison between obese and non-obese patients in multiple sclerosis**:**

Variable	Obese (N=26) BMI≥30	Non-Obese (N=34) BMI<30	Test of significant	*P*-value
Age	33.15 ±9.44	30.06±7.40	1.379	**0.175**
Gender: N (%)			3.279	**0.070**
Male	5(19.23%)	14(41.17%)		
Female	21(80.76%)	20(58.82%)		
Age of disease onset	26.92 ±8.95	27.15±7.35	0.104	**0.918**
Disease Duration	6.23 ±4.65	2.91 ±2.39	3.593	**0.001***
Number of relapses	3.73 ±1.59	3.18 ±1.03	1.636	**0.107**
Fasting blood sugar(mg/dl)	160.88±92.86	126.21±70.13	1.649	**0.105**
Total Cholesterol(mg/dl)	209.35±27.36	182.08±39.13	3.030	**0.004***
Triglyceride (mg/dl)	141.53±40.51	141.15±42.96	0.035	**0.972**
LDL[A] (mg/dl)	131.66±32.25	114.77±33.67	1.972	**0.054**
HDL[A] (mg/dl)	41.14±12.78	46.76±13.70	1.635	**0.108**
EDSS[A]	4.0±2.21	1.89 ±0.88	5.055	**0.001***
MRI activity	**19(73.07%)**	**26(76.47%)**	**0.090**	**0.764**

N: number; A: Mean ±SD; SD: stander deviation; BMI: Body mass index; LDL: low density lipoprotein; HDL: high density lipoprotein; EDSS: Expanded Disability Status Scale; *: significant

Table (3) Correlation between body mass index and other variables**:**

Variable	r	*P*
Age	**0.246**	**0.058**
Age of disease onset	**0.057**	**0.665**
Disease duration	**0.414**	**0.001***
EDSS	**0.629**	**0.001***
Fasting Blood Sugar	**0.386**	**0.002***
Number of Relapse	**0.365**	**0.004***
Triglyceride	**0.048**	**0.714**
Total Cholesterol	**0.425**	**0.001***

EDSS: Expanded Disability Status Scale; *: significant

Table (4) Multivariable logistic regression analysis of factors affecting obesity:

Variable	OR	CI(95%)	P
Number of Relapse	**0.417**	**0.161-1.080**	**0.072**
Disease Duration	**1.185**	**0.897-1.564**	**0.232**
EDSS	**2.837**	**1.209-6.659**	**0.017***
Fasting Blood Sugar	**1.001**	**0.991-1.010**	**0.910**
Total Cholesterol	**1.022**	**0.998-1.046**	**0.074**

OR: odds ratio; CI: confidence interval; EDSS: Expanded Disability Status Scale; *: significant

DISCUSSION

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS), mainly characterized by inflammatory demyelination, diffuse damage and brain volume loss, both of which accounting for neurodegeneration, leading to physical disability [12]. Obesity induces chronic low grade inflammatory conditions that affect innate and adaptive immunity. The increased frequency of both MS and obesity has prompted researchers to look for similar underlying processes. Our aim was to determine the frequency of obesity in MS patients and its relation to disease disability measured by EDSS.

The frequency of obesity among MS patients in this study was 43.3% of patients. Our findings matched the results of other researches that found a higher frequency of overweight and obesity among MS patients [5, 13]. In MS patients, however, a low frequency of 22.5 percent was recorded [6]. This difference may be explained by differences in inclusion criteria of MS, methods of detection of obesity and overweight as well as geographical distribution. Obesity appears to have a key role in the clinical manifestations of MS, particularly in terms of insulin resistance and inflammation [14].

Moreover, in this study, the frequency of obesity was predominant among females in MS patients. Obesity is more common in women than in males, both in rural and urban areas [15]. Obesity prevalence in Middle Eastern countries was similar to that in the United States, with a reported prevalence of 32.1 % to 42.7 % in women and 20.7–37.2 % in males [16]. In contrast, the Macau health survey found that men were twice as likely as women to be obese [17]. Interestingly, studies from the European Union reported a lower prevalence of obesity with little sex disparity as men were found to have a slightly higher prevalence in reports from France and Greece [18]. This imbalance between men and women may be due to variances in muscle mass, obesity, and hormones, which cause metabolic regulation to differ significantly in men and women. Women have a larger body fat percentage, lower lean mass, greater subcutaneous adipose tissue (abdominal and gluteofemoral regions), and higher insulin sensitivity than men. Men, on the other hand, have more visceral fat, greater lean mass, and are less insulin sensitive [19].

When it comes to the link between obesity and disease disability (EDSS), there have been conflicting results. Some studies found no link between obesity and disease disability, whereas others identified a link between both of them. Multiple regression analysis of our MS patients showed that obesity was statistically significant associated with disease disability (EDSS). Our result is in agreement with previous studies [20, 21]. Tettey et al.[22] reported in a regression analysis a significant higher level of disability as measured by EDSS in MS patients who reported obesity compared to those who did not report obesity. In MS patients, a higher BMI was linked to more disability [23-26]. However, Pilutti et al.[27] reported no significant relation between BMI and disability. Obesity represents a proinflamatory condition characterized by increased expression of inflammatory mediators, including interleukin (IL)-6 and leptin [21]. Altered lipid metabolism has been associated with worse disease course in MS patients [28]. Moreover, increased BMI has been associated with lower response to interferon-β (IFN-β) therapy in MS patients [25]. There has recently been evidence that a greater BMI in MS patients is linked to greater grey matter atrophy [29].

CONCLUSION

Obesity was shown to be common among MS patients in this study. Obesity was found to be significantly linked with disease disability (EDSS) in MS patients. Obesity screening should be included in MS care in order to identify high-risk patients and educate MS patients on how to prevent weight gain.

RECOMMENDATIONS

Obesity screening should be a regular component of MS management that could help in

identification of high risk patients and improve clinical decision- practice. Further prospective studies are needed to validate association between obesity and disease progression in MS patients for better application in clinical practice.

Conflict of interest: No.

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REFERENCES

1. Azimi M, Ghabaee M, Moghadasi AN, Noorbakhsh F, Izad M. Immunomodulatory function of Treg-derived exosomes is impaired in patients with relapsing-remitting multiple sclerosis. Immunol Res. 2018;66(4):513-520. doi:10.1007/s12026-018-9008-5.
2. Guzel I, Mungan S, Oztekin ZN, Ak F. Is there an association between the Expanded Disability Status Scale and inflammatory markers in multiple sclerosis? J Chinese Med Assoc. 2016;79(2):54-57. doi:10.1016/j.jcma.2015.08.010.
3. Palavra F, Almeida L, Ambrósio AF, Reis F. Obesity and brain inflammation: A focus on multiple sclerosis. Obes Rev. 2016;17(3):211-224. doi:10.1111/obr.12363.
4. Negrotto L, Farez MF, Correale J. Immunologic effects of metformin and pioglitazone treatment on metabolic syndrome and multiple sclerosis. JAMA Neurol. 2016;73(5):520-528. doi:10.1001/jamaneurol.2015.4807.
5. Pinhas-Hamiel O, Livne M, Harari G, Achiron A. Prevalence of overweight, obesity and metabolic syndrome components in multiple sclerosis patients with significant disability. Eur J Neurol. 2015;22(9):1275-1279. doi:10.1111/ene.12738.
6. Sicras-Mainar A, Ruíz-Beato E, Navarro-Artieda R, Maurino J. Comorbidity and metabolic syndrome in patients with multiple sclerosis from Asturias and Catalonia, Spain. BMC Neurol. 2017;17(1):1-6. doi:10.1186/s12883-017-0914-2.
7. Barcellos L. Obesity and Multiple Sclerosis Susceptibility: A Review. J Neurol Neuromedicine. 2016;1(7):1-5. doi:10.29245/2572.942x/2016/7.1064.
8. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, et al. Diagnostic criteria for multiple sclerosis: 2010 Revisions to the McDonald criteria. Ann Neurol. 2011;69(2):292-302. doi:10.1002/ana.22366.
9. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018;17(2):162-173. doi:10.1016/S1474-4422(17)30470-2.
10. JF K. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology. 1983;33(11):1444-52.
11. Hurria A, Cohen HJ, Extermann M. WHO_TRS_854.pdf. J Geriatr Oncol. 2010;1(1):40-44. https://www.analesdepediatria.org/en-tuberculosis-in-paediatric-age-group-articulo-S2341287920302544.
12. Gholamzad M, Ebtekar 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;68(1):25-38. doi:10.1007/s00011-018-1185-0.
13. Slawta JN, Wilcox AR, Mccubbin JA, Nalle DJ, Fox SD, Anderson G. Health Behaviors , Body Composition , and Coronary Heart Disease Risk in Women With Multiple Sclerosis. 2003;84(12):1823-1830. doi:10.1016/S0003-9993(03)00466-0.
14. Uize LOG. All-Cause Mortality Associated With Specific Combinations of the Metabolic. 2007;30(9), 2381-2387. doi:10.2337/dc07-0186.Abbreviations.
15. Cherry CO, Serieux E, Didier M, Nuttal ME, Schuster RJ. Prevalence of Risk Factors for the Metabolic Syndrome in the Middle Income Caribbean Nation of St. Lucia. Adv Prev Med. 2014;2014:1-5. doi:10.1155/2014/501972.
16. Mabry RM, Reeves MM, Eakin EG, Owen N. Gender differences in prevalence of the metabolic syndrome in Gulf Cooperation Council Countries: A systematic review. Diabet Med. 2010;27(5):593-597. doi:10.1111/j.1464-5491.2010.02998.x.
17. Sobko T, Trindade D, Lao QX, Wong M, Io TK, Wa CK, et al. Men in Macau SAR have higher prevalence in metabolic syndrome and among related metabolic components: A cross-sectional Macau Health Survey. BMC Public Health. 2014;14(1):1-8. doi:10.1186/1471-2458-14-1065.
18. Kapitza C, Forst T, Coester H V., Poitiers F, Ruus P, Hincelin-Méry. A Pharmacodynamic characteristics of lixisenatide once daily versus liraglutide once daily in patients with type 2 diabetes insufficiently controlled on metformin. Diabetes, Obes Metab. 2013;15(7):642-649. doi:10.1111/dom.12076.
19. Varlamov O, Bethea CL, Roberts CT. Sex-specific differences in lipid and glucose metabolism. Front Endocrinol (Lausanne). 2014:5, 1-7. doi:10.3389/fendo.2014.00241.
20. Carriere I, Pérès K, Ancelin ML, Gourlet V, Berr C, Barberger-Gateau P, et al. Metabolic syndrome and disability: Findings from the prospective three-city study. Journals Gerontol - Ser A Biol Sci Med Sci. 2014;69(1):79-86. doi:10.1093/gerona/glt101.
21. Stampanoni Bassi M, Iezzi E, Buttari F, Gilio L, Simonelli I, Carbone F ,et al. Obesity worsens central inflammation and disability in multiple sclerosis. Mult Scler J. 2019:1-10. doi:10.1177/1352458519853473.
22. Tettey P, Siejka D, Simpson S, Taylor B, Blizzard L, Ponsonby AL ,et al. Frequency of comorbidities and their association with clinical disability and relapse in multiple sclerosis. Neuroepidemiology. 2016;46(2):106-113. doi:10.1159/000442203.
23. Oliveira SR, Colado Simão AN, Kallaur AP, de Almeida ERD, Morimoto HK, Lopes J ,et al. Disability in patients with multiple sclerosis: Influence of insulin resistance, adiposity, and

oxidative stress. Nutrition. 2014; 30(3):268-273. doi:10.1016/j.nut.2013.08.001.
24. Tettey P, Simpson S, Taylor B, Ponsonby A L, Lucas RM, Dwyer T ,et al. An adverse lipid profile and increased levels of adiposity significantly predict clinical course after a first demyelinating event. J.Neurol Neurosurg. Psychiatry, 2017; 88:395-401.
25. Kvistad SS, Myhr KM, Holmøy T, Benth JŠ, Wergeland S, Beiske AG ,et al. Body mass index influence interferon-beta treatment response in multiple sclerosis. J Neuroimmunol. 2015;288:92-97. doi:10.1016/j.jneuroim.2015.09.008.
26. Fahmi RM, El Ebeary MES, Abd Alrasheed EM, Elkhatib THM. Metabolic syndrome components and disease disability in egyptian multiple sclerosis patients. Mult Scler Relat Disord. 2020;44(6):102336. doi:10.1016/j.msard.2020.102336.
27. Gokhale AM, Patel GR. Analysis of variability in tensile ductility of a semi-solid metal cast A356 Al-alloy. Mater Sci Eng A. 2005;392(1-2):184-190. doi:10.1016/j.msea.2004.09.051.
28. Tettey P, Van Der Mei IAF. Lipids in multiple sclerosis: Adverse lipid profiles, disability and disease progression. Clin Lipidol. 2014;9(5):473-475. doi:10.2217/clp.14.41.
29. Mowry EM, Azevedo CJ, Mcculloch CE, Okuda DT, Lincoln RR, Waubant E ,et al. Body mass index, but not Vitamin D status, is associated with brain volume change in MS. Neurology. 2018;91(24): e2256-e2264. doi:10.1212/WNL.0000000000006644.

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