The Comparison of the Lipid Profiles of the Overweighted/ Obese and Normal Weighted Male and Female Patients with Multiple Sclerosis (MS): A Cross Sectional Pilot Study

Multiple Sklerozlu (MS) Hafif Şişman, Obez ve Normal Vücut Ağırlıklı Erkek ve Kadın Hastaların Lipid Profillerinin Karşılaştırılması: Kesitsel Bir Pilot Çalışma

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ABSTRACT

Aim: *The aim of the study was to determine the overweight/obesity status, plasma total cholesterol and triglyceride levels in multiple sclerosis (MS) patients.* ***Subjects and Methods:*** *This study was conducted on 63 MS patients (41 female, 22 male) who have applied to Ankara Numune Education and Research Hospital, Department of Neurology. Body composition analysis [body fat mass (kg), body fat percentage (%), fat free mass (kg) and body water (kg)] was measured by bioelectrical impedance analyzer (BIA) at the Department of Nutrition and Dietetics in Gazi University. The lipid profile [total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), very low-density lipoprotein-cholesterol (VLDL-C) and triglyceride (TG)] of each participant was measured.* ***Results:*** *The mean age was found 35.1 ± 8.90 years for females, 34.6 ± 8.19 years for males (20-56 years). Overweight/obesity was found more prevalent in females than in males (41.5% of the females and 36.3% of the males had higher body mass index (BMI) (>25.0 kg/m^2), respectively). While the body fat mass (FM) (p= 0.048) and fat percentage (FP) (p< 0.001) measurements were high in females; fat free mass (FFM) (p<0.001) and total body water (p<0.001) measurements were found to be higher in males.* ***Conclusion:*** *It was concluded that obesity was more prevalent in females and was also a risk factor for cardiovascular diseases in MS subjects in this study.*

Keywords: *Multiple sclerosis (MS), overweight, obesity, lipid profile*

ÖZET

Amaç: *Bu çalışmada, multiple skleroz (MS) hastalarında hafif şişmanlık /şişmanlık durumuna göre, plazma toplam kolesterol ve trigliserit düzeylerinin belirlenmesi amaçlanmıştır.* ***Bireyler ve Yöntem:*** *Bu çalışma, Ankara Numune Eğitim ve Araştırma Hastanesi, Nöroloji Anabilim Dalı'na başvuran 63 MS hastası (41 kadın birey, 22 erkek birey) üzerinde gerçekleştirilmiştir. Vücut bileşim analizi [vücut yağ kütlesi (kg), vücut yağ yüzdesi (%), yağsız doku kütlesi (kg) ve vücut suyu (kg)] Gazi Üniversitesi Beslenme ve Diyetetik Bölümü'nde biyoelektrik impedans analizörü (BİA) kullanılarak ölçülmüştür. Her katılımcının lipit profili [total kolesterol (TK), yüksek yoğunluklu lipoprotein-kolesterol (HDL-K), düşük yoğunluklu lipoprotein-kolesterol (LDL-K), çok düşük yoğunluklu lipoprotein - kolesterol (VLDL-K) ve trigliserit TG)] düzeyleri ölçüldü.* ***Bulgular:*** *Yaş ortalaması kadınlarda 34.6 ± 8.19 yıl, erkeklerde 35.1 ± 8.90 yıl (20-56 yıl) olarak bulunmuştur. Kadınlarda hafif şişmanlık/ şişmanlık sıklığı erkeklerden daha yüksektir (sırasıyla kadınların %41.5'inin ve erkeklerin %36.3'ünün beden kütle indeksi (BKİ) yüksektir (>25.0 kg/m^2). Kadınlarda vücut yağ kütlesi (FM) (kg) (p= 0.048) ve vücut yağ oranı (FP) (%) (p<0.001) ölçümleri daha yüksek iken, erkeklerde yağsız doku kütlesi (FFM) (kg) (p<0.001) ve total vücut suyu (kg) (p<0.001) ölçümleri daha yüksek bulunmuştur.* ***Sonuç:*** *Bu çalışmada, MS hastalarında şişmanlığın kadınlarda daha yaygın olduğu ve aynı zamanda kardiyovasküler hastalıklar için bir risk etmeni olduğu sonucuna varılmıştır.*

Anahtar kelimeler: *Multiple skleroz (MS), hafif şişmanlık, şişmanlık lipit profili*

INTRODUCTION

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system that causes neurological impairment which mainly affects adults (1,2). MS is more common among women than men. The disease has a prevalence of 30-80 per 100.000 in Canada, Northern Europe and the United States (3).

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Obesity is associated with a low-grade chronic inflammatory state and release of cytokines that affect immune responses and possibly MS risk (4). The relationship between obesity during adolescence and multiple sclerosis (MS) risk has previously been investi¬gated using two large cohorts of American women in which obese female adolescents displayed an increased risk of developing MS (5). Women who reported higher weight in adolescence and body mass index (BMI) in early adulthood were younger at MS onset (6). The normal BMI range, as defined by the World Health Organization (WHO), is quite wide, and some people within this range may have excessive central fat accumulation and elevated metabolic risks. Cambil-Martín et al. (7) found overweight MS patients evidenced higher depression levels, lower functional capacity, and worse self-rated health status in comparison to normal-weight MS patients. The waist-to-height ratio (WHtR), an effective index for assessing central fat distribution, can be used to identify subjects who are at higher metabolic risk within the normal as well as the overweight range (8).

The present study was conducted in order to determine the overweight / obesity status and plasma cholesterol and triglyceride levels in Multiple sclerosis (MS) patients.

SUBJECTS and METHODS

This study was conducted on 63 MS patients (41 female, 22 male) who have applied to Ankara Numune Education and Research Hospital, Department of Neurology, Turkey from April to July 2012. The disease was diagnosed by a neurologist. Pregnant women, habitual smokers, chronic alcohol consumers, and consumers of vitamin and mineral supplements were excluded from the study. Among the cases, individuals with other disorders in addition to MS were also excluded. The participants were informed about the subject and the purpose of the research. Each participant signed a voluntary participation form and gave informed written consent which adhered to Declaration of Helsinki Protocols (World Medical Association).

Body composition analysis was measured by bioelectrical impedance analyzer (BIA: Tanita TBF 300). All anthropometric measurements were taken by trained dietitians. During the measurement process, participants wore light clothes and had bare feet. A portable scale was used to measure body weight to the nearest half-kilogram. Height was measured to the nearest 0.1 cm with a wall-mounted stadiometer. Body mass index (BMI, kg/m^2) was calculated by weight in kilograms divided by the square of height in meters. The patients were classified according to their BMI into four groups: underweight (BMI<18.5 kg/m^2), normal weight (BMI: 18.5 to 24.9 kg/m^2), overweight (BMI: 25.0 to 29.0 kg/m^2) and obese (BMI ≥30 kg/m^2) (9). Waist circumference was measured at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest at minimum respiration (10). Waist-to-height ratio (WHtR) was also calculated.

The lipid profile included total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), very low-density lipoprotein-cholesterol (VLDL-C) and triglyceride (TG). Early-morning venous blood samples were obtained from each participant for biochemical screening tests after eight hour fasting, following a twelve-hour overnight fast. Professional staff performed venipuncture using vacutainers to obtain 15 mL of whole blood. Serum cholesterol analyses were performed in Numune Hospital. Roche Diagnostic Kits were used for TG, HDL-C and TC analysis. The LDL-C was calculated by the formula by Friedewald and colleagues; LDL-C= TC - (HDL-C + (TG/5) (11).

RESULTS

The Relapsing/Remitting Multiple Sclerosis (RRMS) was mostly seen (90.5%) in both of the genders. Only the 4.9% of the females and 13.6% of the males were diagnosed as Secondary Progressive Multiple Sclerosis (SPMS). When patients were evaluated to the year of diagnosis, approximately only 10% of the whole group (9.7% females, 9.0% males) was over 10 years of diagnosis.

This study was conducted on 63 (41 females, 22 males) MS patients between the ages of 20-56 years. The mean age was found 35.1±8.90 years for females, 34.6±8.19 years for males. The most of the females (80.5%) and 68.2% of the males were married. The educational status of the males was found higher than the females. The 63.7% of the males were graduated from high school and/or

Table 1. The evaluation of body weight status of the patients (n= 63)

BMI classification	Female		Male		Total	
	n	%	n	%	n	%
Underweight	3	7.3	3	13.6	6	9.5
Normal weight	21	51.2	11	50.0	32	50.8
Overweight	10	24.4	7	31.8	17	27.0
Obese	7	17.1	1	4.5	8	12.7

Table 2. Some anthropometric and biochemical parameters of the patients

Parameters	Female (n= 41) Mean ± SD	Male (n= 22) Mean ± SD	Total (n= 63) Mean ± SD	p
BW(kg)	64.7±11.19	76.9±14.03	68.9±13.49	0.001*
BMI (kg/m2)	25.4±4.89	24.8±4.89	25.2±4.86	0.677
BMR (kcal)	1356.6±130.07	1788.4±254.99	1507.4±275.70	0.001*
FM (kg)	20.2±7.91	15.6±8.93	18.6±8.50	0.048**
FP (%)	30.5±7.51	19.5±8.80	16.7±9.52	<0.001*
FFM (kg)	44.5±4.38	60.9±8.53	50.2±9.95	<0.001*
TBW(kg)	32.6±3.20	44.6±6.25	36.8±7.30	<0.001*
WC (cm)	85.7±11.68	89.7±12.72	87.1±12.10	0.232
WHR	0.80±0.06	0.87±0.06	0.82±0.06	<0.001*
WHtR	0.53±0.08	0.51±0.07	0.52±0.07	0.199
TC (mg/dL)	179.5±48.11	178.3±35.28	179.1±43.77	0.913
LDL-C (mg/dL)	100.6±41.67	103.9±28.32	101.7±37.34	0.716
HDL-C (mg/dL)	58.4±15.82	43.9±10.86	53.4±15.80	<0.001*
VLDL-C (mg/dL)	20.4±10.27	31.5±20.17	24.3±15.31	0.022**
TG (mg/dL)	102.5±51.18	157.6±100.89	121.7±76.41	0.024**

BW: Body weight, BMI: Body mass index, BMR: Basal metabolic rate, FM: Fat mass, FP: Fat percentage, FFM: Fat free mass, TBW: Total body water, WC: Waist Circumstance, WHR: Waist hip ratio, WHtR: waist-to-height ratio, TC: Total cholesterol, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, VLDL-C: Very low density lipoprotein cholesterol *p<0.001, ** p<0.05

had bachelor's degree while most of the females were graduated from primary school (36.6%). When the individuals were evaluated according to their professions, the majority of the females were housewife (73.2%) and only 18.2% of the males were found retired.

The 50.8% of the MS patients had normal weight, 27.0% were overweight and 12.7% were obese (Table 1). Overweight/obesity was more prevalent in females than in males (41.5% of the females and 36.3% of the males had higher BMIs (>25.0 kg/m^2), respectively).

Table 2 shows the anthropometric measurements of the study group measured by BIA. Although the mean Body Mass Index (BMI-kg/m^2) did not differ in both genders (25.4±4.89 kg/m^2 for females and 24.8±4.89 kg/m^2 for males, respectively) (p>0.05), the mean body weight (BW) and waist-hip ratio (WHR) and basal metabolic rate (BMR) measurements were found to be significantly higher in males than females (p=0.001). While the body fat mass (FM) (p=0.048) and fat percentage (FP) (p<0.001) was higher in females; fat free mass (FFM) (p<0.001) and total body water (TBW) (p<0.001) measurements were found to be higher in males. While the mean VLDL-C (p=0.022) and TG (p=0.024) was significantly lower in females; HDL-C (p<0.001) level was higher (p<0.001).

It was found that while the TC, LDL-C and HDL-C levels were high in BMI ≥25 kg/m^2 in both genders; the VLDL-C and TG levels was lower only in males (Table 3).

Table 3. The lipid profile of the patients according to the BMI (kg/m^2) levels

Biochemical parameters	Female		Male	
	<25 kg/m^2 Median	≥25 kg/m^2 Median	<25 kg/m^2 Median	≥25 kg/m^2 Median
TC (mg/dL)	163.0	170.5	175.0	187.5
LDL-C (mg/dL)	89.0	100.0	102.5	111.5
HDL-C (mg/dL)	53.0	53.5	44.0	42.5
VLDL-C (mg/dL)	18.0	19.5	28.0	24.0
TG (mg/dL)	91.0	97.0	139.0	120.5

DISCUSSION

There are multiple genetic factors affecting risk of developing MS and disease severity. There is a rising worldwide prevalence and the increasing female to male preponderance has focused interest on environmental factors influencing MS risk. Data on these factors that particular focus on such as vitamin intake, smoking and obesity, which may be influenced at a personal and population level by medical advice (12). As MS is more common in females than males and frequently affects women during their reproductive years (3,13), the majority of the present study sample consists females (65%).

Smoking and lifestyle factors that are related with overweight/obesity (such as unhealthy diet and physical inactivity) appear to play a major role in morbidity and mortality among persons with serious mental illnesses. Compton et al. (14) found that individuals who have mental illnesses are more than twice as likely to smoke and more than 50% more likely to be overweight / obese. Patients with MS often have a history of smoking and overweight or obesity (15). In this present study, the 25% of the females and 41% of the males were smoking. Only 18% of the males have declared to give up smoking after the diagnosis of MS. The majority of the females reported that they have never smoked. When MS is newly diagnosed, a substantial proportion of affected individuals have physical and mental comorbidities. Comorbidity may be associated with the clinical phenotype of the disease and may affect prognostication and treatment decisions (16-18).

In the present study, we found that 39.7% of the participants were overweight / obese and it was more prevalent in females (41.5%) than in males. This was an important result since Hedström et al. (17) found that higher BMI results in a higher risk of developing MS. In addition to these results, Munger et al. (5) also declared that over¬weight and obese subjects at age 20 had an increased risk of developing MS when compared to with normal weight subjects.

Obesity is associated with a low-grade inflammation of white adipose tissue (WAT) resulting from chronic activation of the immune system. This situation subsequently lead to insulin resistance, impaired glucose tolerance and even diabetes. White adipose tissue is the physiological site of energy storage as lipids. In addition, it has been more recently recognized as an active organ in numerous physiological and pathophysiological processes. In obesity, WAT is characterized by an increased production and secretion of a wide range of inflammatory molecules including TNF-alpha and interleukin-6 (IL-6), which may have local effects on WAT physiology as well as systemic effects on other organs. Recent data indicate that obese WAT is infiltrated by macrophages, which may be a major source of locally-produced pro-inflammatory cytokines (19). Central obesity has been associated with increased risk of cardiovascular and metabolic disease in adults. Anthropometric indices predictive of central obesity include WC, WHR and WHtR (20). In this study, while the FM and FP was higher in females; FFM measurements were found to be lower ($p<0.05$). Waist to height ratio, which is a significant predictor of chronic diseases risk factors (21), was higher in the females than in males although this did not reach to statistical difference. This means that central obesity was seen more prevalent in the females. The molecular path¬ways responsible for the observed association between obe¬sity and MS are not known yet, but there are different hypotheses attempting to explain this association. Increasing the production and release of pro-inflam¬matory cytokines and promoting Th1 responses, characterized by the production of interferon-gamma, and decreasing the number of regulatory T-cells, obesity may either increase the risk of recruitment of auto-immune CD4 cells (a co-receptor that assists the T cell receptor) that target neuro-protective effects of immunization with self-CNS antigens, or alternatively bias their cytokine differentiation pattern into a more path¬ogenic profile (17).

Multiple sclerosis is also characterized by the destruction of myelin. Marked alterations in both myelin cholesterol and lipid metabolism occur in the central nervous system (21). Multiple sclerosis

patients exhibit a decrease in neuroprotective and immunoregulatory vitamins and an increase in TC and HDL-C which may be associated with the different phases of the disease (22). Increased values of total and HDL-C were reported in a study which aimed to assess the correlation between serum TC and magnetic resonance imaging (MRI) activity after a clinical episode suggesting MS. In the present study HDL-C levels was found significantly higher in females than the males and also TC and LDL-C was low in both of the genders. This shows us that the lipid profiles of the study group were between the suggested levels. Another important finding of this study was that while BMI was increasing, the serum TC, LDL-C and TG levels were also increasing. This means that obesity is also a risk factor for cardiovascular diseases in MS subjects. Besides this, the pathogenetic mechanisms underlying the changes in the plasma lipid profile are not clear (22), but it is well-known that the development of MS plaques is associated with the activation of a large number of mediators, including cytokines and anaphylatoxins, known to induce changes in the capacity of the liver to synthesize plasma lipoproteins (23). Giubilei et al. (21) indicated that plasma levels of total and LDL-C are of practical use in monitoring the disease course in MS.

As a conclusion, obesity is more prevalent in females and is also a risk factor for cardiovascular diseases in MS subjects. Central obesity was seen more prevalent in the females. An adequate and balanced diet combined with a regular physical activity in MS patients is an important strategy for providing a healthy life and improved quality of life (QoL). Further research is needed to understand the associations between obesity and MS and their mechanisms and also the effect of inflammation.

Conflict of interest: *There is no conflict of interest.*

Limitation: *The study's main weakness is its limited sample size and it must therefore be regarded as preliminary to larger investigations.*

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KAYNAKLAR

1. Castro-Borrero W, Graves D, Frohman TC, Flores AB, Hardeman P, Logan D, et al. Current and emerging therapies in multiple sclerosis: a systematic review. Ther Adv Neurol Disord 2012;5(4):205-220.
2. Hersh C, Rae-Grant A. Extended-release dalfampridine in the management of multiple-sclerosis-related walking impairment. Ther Adv Neurol Disord 2012;5(4):199-204.
3. Mirza M. The etiology and the epidemiology of multiple sclerosis. Erciyes Medical Journal 2002;24(1):40-47.
4. Maffei M, Halaas J, Ravussin E, Pratley RE, Lee GH, Zhang Y, et al. Leptin levels in human and rodent: measurement of plasma leptin and ob RNA in obese and weight-reduced subjects. Nat Med 1995;1:1155–1161.
5. Munger KL, Chitnis T and Ascherio A. Body size and risk of MS in two cohorts of US women. Neurology 2009;73:1543–1550.
6. Kavak KS, Teter BE, Hagemeier J, Zakalik K, Weinstock-Guttman B. Higher weight in adolescence and young adulthood is associated with an earlier age at multiple sclerosis onset. Mult Scler. 2014 [Epub ahead of print].
7. Cambil-Martín J, Galiano-Castillo N, Muñoz-Hellín E, Díaz-Rodríguez L, Laguarta-Val S, Fernández-de-Las-Peñas C, et al. Ifluence of body mass index on psychological and functional outcomes in patients with multiple sclerosis: a cross -sectional study. Nutr Neurosci. 2014 [Epub ahead of print]
8. Hsieh SD, Yoshinaga H, Muto T. Waist-to-height ratio, a simple and practical index for assessing central fat distribution and metabolic risk in Japanese men and women. Int J Obes Relat Metab Disord 2003;27(5):610-616.
9. WHO/FAO. Diet, Nutrition and the Prevention of Chronic Diseases, WHO Technical Report Series, 916, Geneva, 2003.
10. Lohman TG, Roche AF, Martorell R. Anthropometric Standardization Reference Manual. Kinetics Books, Champaign, Illinois, pp. 1-50, 1988.
11. Friedewald WT, Levy RI, Fedickso DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of preparative ultracentrifuge. Clin Chem 1972;18,499-502.
12. Young CA. Factors predisposing to the development of multiple sclerosis. QJM 2011;104(5):383-386.
13. McCombe PA, Greer JM. Female reproductive issues in multiple sclerosis. Mult Scler 2013;19(4):392-402.
14. Compton MT, Daumit GL, Druss BG. Cigarette smoking and overweight/obesity among individuals with serious mental illnesses: a preventive perspective. Harv Rev Psychiatry 2006;14(4):212-222.
15. Marrie RA, Horwitz RI, Cutter G, Tyry T, Vollmer T. Association between comorbidity and clinical characteristics of MS. Acta Neurol Scand 2011;124(2):135-141.
16. Marrie RA, Horwitz RI. Emerging effects of comorbidities on multiple sclerosis. Lancet Neurol 2010;9(8):820-828.
17. Hedström AK, Olsson T, Alfredsson L. High body mass index before age 20 is associated with increased risk for multiple sclerosis in both men and women. Mult Scler 2012;18:1334-1336.
18. Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H, et al. Recent advances in the relationship

between obesity, inflammation, and insulin resistance. Eur Cytokine Netw 2006;17(1):4-12.
19. Yong L, Guanghui T, Weiwei , Liping L,, Xiaosong Q. Can body mass index, waist circumference, waist-hip ratio and waist-height ratio predict the presence of multiple metabolic risk factors in Chinese subjects? BMC Public Health 2011; 11: 35.
20. David J, Tybor AH, Lichtenstein GE, Dallal AM. Waist-to-height ratio is correlated with height in US children and adolescents aged 2–18 years. Int J Pediatr Obes 2008;(3):148–51.
21. Giubilei F, Antonini G, Di Legge S, Sormani MP, Pantano P, Antonini R, et al. Blood cholesterol and MRI activity in first clinical episode suggestive of multiple sclerosis. Acta Neurologica Scandinavica 2002;106:109–112.
22. Salemi G, Gueli MC, Vitale F, Battaglieri F, Guglielmini E, Ragonese P, et al. Blood lipids, homocysteine, stress factors, and vitamins in clinically stable multiple sclerosis patients. Lipids Health Dis. 2010;9:19.
23. Wekerle H. The immunology of multiple sclerosis. In: Compston A, ed. McAlpine's multiple sclerosis. London: Churchill Livingstone, 1998;379–407.