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Impact of Adiposity, Insulin Resistance, and Lipid Profile on Clinical Characteristics in Patients with Relapsing– Remitting Multiple Sclerosis

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Research Article

Keywords: Multiple sclerosis, insulin resistance, lipid profile, adiposity, body mass index

Posted Date: March 17th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9074642/v1

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Additional Declarations: No competing interests reported.

Abstract

Objective

Metabolic disturbances have increasingly been recognized as potential modifiers of disease course in multiple sclerosis (MS). This study aimed to evaluate insulin resistance, anthropometric parameters, and lipid profiles in patients with relapsing–remitting MS (RRMS) and to investigate their association with clinical disability.

Methods

This single-center prospective case–control study included 70 RRMS patients diagnosed according to the 2017 revised McDonald criteria and 70 age-matched healthy controls. Demographic characteristics, anthropometric measurements (body mass index and waist circumference), biochemical markers related to insulin resistance, and lipid profile parameters were recorded. Insulin resistance was assessed using the homeostatic model assessment (HOMA-IR). Multivariate regression analyses were performed to explore independent predictors of insulin resistance and disability measured with the Expanded Disability Status Scale (EDSS).

Results

Compared with healthy controls, patients with RRMS had significantly higher body weight, body mass index, and waist circumference. Total cholesterol and HDL-cholesterol levels were also significantly higher in the MS group. However, fasting glucose, fasting insulin, and HOMA-IR values were comparable between groups. Multivariate regression analysis demonstrated that waist circumference was independently associated with HOMA-IR values. Among MS patients, those with insulin resistance showed significantly higher triglyceride levels. Patients with abdominal obesity and elevated BMI demonstrated significantly higher total cholesterol and LDL-cholesterol levels. No independent association was observed between lipid profile parameters or insulin resistance and EDSS scores. Triglyceride levels were significantly lower in patients receiving dimethyl fumarate therapy compared with those treated with fingolimod or ocrelizumab.

Conclusion

RRMS patients exhibit increased adiposity and alterations in lipid metabolism compared with healthy individuals. These metabolic changes appear to be primarily associated with adiposity rather than insulin resistance. Although lipid abnormalities were not independently associated with disability in this cohort, metabolic alterations may still represent important comorbid factors in MS and warrant further investigation in larger longitudinal studies.

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative disease of the central nervous system characterized by immune-mediated demyelination and axonal damage (1). The relapsing–remitting form (RRMS) accounts for approximately 85% of all MS cases at disease onset (1). In recent years, increasing attention has been directed toward the role of systemic comorbidities and metabolic factors in influencing disease activity and progression (2).

Metabolic disturbances including obesity, dyslipidemia, and insulin resistance have been proposed as potential contributors to neuroinflammation and neurodegeneration (3).

Metabolic disturbances including obesity, dyslipidemia, and insulin resistance have been proposed as potential contributors to neuroinflammation and neurodegeneration. Adipose tissue functions as an active endocrine organ that secretes adipokines and inflammatory mediators capable of modulating immune responses. Consequently, increased adiposity may promote systemic inflammation and potentially influence autoimmune diseases such as MS.

Previous studies have demonstrated associations between obesity and increased risk of MS as well as potential relationships between lipid metabolism and disease activity. Dyslipidemia has also been suggested to contribute to vascular dysfunction and chronic inflammatory processes that may aggravate neurological disability. However, data regarding the relationship between insulin resistance, lipid metabolism, and clinical disability in MS remain inconsistent.

Understanding metabolic alterations in MS patients may provide valuable insight into potentially modifiable factors affecting disease course. Therefore, the present study aimed to evaluate anthropometric parameters, insulin resistance, and lipid profile characteristics in RRMS patients and to investigate their potential association with disability.

MATERIALS AND METHODS

Study Design

This prospective case–control study was conducted at Gaziantep University Faculty of Medicine. Ethical approval was obtained from the institutional Clinical Research Ethics Committee, and the study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Participants

Seventy patients diagnosed with RRMS according to the 2017 revised McDonald criteria and 70 healthy volunteers were included in the study. Eligible participants were between 18 and 60 years of age. Healthy controls had no history of chronic disease and were not receiving regular medication.

Patients who had received corticosteroid therapy within the preceding three weeks, as well as pregnant or lactating individuals and those with other inflammatory, autoimmune, or neurodegenerative diseases, were excluded from the study.

Anthropometric and Clinical Assessment

Demographic data including age and sex were recorded. Anthropometric measurements included body weight, height, body mass index (BMI), and waist circumference. Disease duration and disease-modifying therapies were documented for all patients. Neurological disability was assessed using the Expanded Disability Status Scale (EDSS).

Laboratory Measurements

Blood samples were obtained following a 12-hour fasting period. Serum glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglyceride levels were measured using an automated biochemical analyzer. Serum insulin levels were determined using chemiluminescent immunoassay methods.

Insulin resistance was estimated using the homeostatic model assessment (HOMA-IR) calculated according to the standard formula.

Statistical Analysis

Statistical analyses were performed using SPSS software. Normality of numerical variables was evaluated with the Shapiro–Wilk test. Continuous variables were compared using Student's t-test or Mann–Whitney U test as appropriate. For comparisons among more than two groups, one-way ANOVA or Kruskal–Wallis tests were applied.

Multivariate linear regression analyses were conducted to determine independent predictors of insulin resistance and EDSS scores. Variables included in regression models were age, disease duration, BMI, waist circumference, and lipid profile parameters. Statistical significance was defined as $p < 0.05$.

RESULTS

Demographic and Anthropometric Characteristics

The study included 70 RRMS patients and 70 healthy controls. The gender distribution was comparable between groups. The mean age of the MS group was higher than that of the control group.

RRMS patients demonstrated significantly higher body weight, waist circumference, and BMI compared with healthy controls.

Biochemical Parameters

Fasting glucose and fasting insulin levels were slightly higher in the MS group but did not reach statistical significance. Similarly, HOMA-IR values were comparable between patients and controls.

In contrast, lipid profile analysis revealed significantly higher total cholesterol and HDL-cholesterol levels in the MS group. LDL-cholesterol and triglyceride levels also tended to be higher among MS patients, although these differences did not reach statistical significance.

Multivariate regression analysis revealed that waist circumference was independently associated with HOMA-IR values after adjustment for age and disease status.

Insulin Resistance Subgroup Analysis

When MS patients were stratified according to insulin resistance status, triglyceride levels were significantly higher in the insulin-resistant group. No significant differences were observed in age, disease duration, or EDSS scores.

Abdominal Obesity and BMI Subgroups

Patients with abdominal obesity demonstrated significantly higher total cholesterol, HDL-cholesterol, and LDL-cholesterol levels compared with those without abdominal obesity.

Similarly, overweight patients according to BMI classification exhibited significantly elevated total cholesterol and LDL-cholesterol levels compared with normal-weight patients.

Disease-Modifying Therapy Analysis

Metabolic parameters were also analyzed according to disease-modifying therapies. No significant differences were observed in glucose metabolism or cholesterol parameters among therapy groups. However, triglyceride levels were significantly lower in patients receiving dimethyl fumarate therapy.

Table 1. General Characteristics of Study Participants

Variable	MS Patients (n=70)	Controls (n=70)	p-value
Age (years)	34.8 ± 9.31	29.63 ± 7.74	0.001
Height (cm)	168.06 ± 9.39	168.74 ± 8.64	0.654
Weight (kg)	75.43 ± 15.5	68.6 ± 12.28	0.006
BMI (kg/m²)	26.81 ± 5.83	24.0 ± 3.29	0.006
Waist circumference (cm)	94.1 ± 13.91	84.04 ± 11.21	0.001

BMI: Body Mass Index; MS: Multiple Sclerosis. Values are presented as mean ± standard deviation.

Table 2. Comparison of Biochemical Parameters

Parameter	MS Patients	Controls	p-value
Fasting glucose	89.74 ± 16.22	87.69 ± 12.74	0.344
Fasting insulin	8.12 ± 4.53	7.94 ± 7.01	0.183
HOMA-IR	1.88 ± 1.49	1.77 ± 1.74	0.092
Total cholesterol	197.61 ± 44.06	180.86 ± 36.28	0.015
HDL-C	57.53 ± 11.97	54.17 ± 12.11	0.029
LDL-C	126.33 ± 34.17	115.77 ± 30.13	0.055
Triglyceride	125.37 ± 81.44	101.67 ± 61.85	0.058

HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol.

Table 3. Multivariate Regression Analysis for HOMA-IR

Variable	B	Std. Error	Beta	p-value
Age	−0.029	0.016	−0.159	0.079
Waist circumference	0.055	0.011	0.462	0.001
Disease status	0.293	0.275	0.091	0.290

Dependent variable: HOMA-IR. B: unstandardized coefficient; Beta: standardized coefficient. The model was adjusted for age, waist circumference, and disease status.

Table 4. Lipid Profile According to Insulin Resistance Status in MS

Parameter	With IR	Without IR	p-value
TC	209.2 ± 49.75	191.57 ± 40.03	0.112
HDL-C	56.33 ± 10.89	58.15 ± 12.56	0.687
LDL-C	135.7 ± 38.42	121.39 ± 31.03	0.094
TG	152.1 ± 88.18	111.41 ± 74.92	0.014

IR: Insulin resistance defined according to HOMA-IR threshold. TC: Total cholesterol; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; TG: Triglycerides.

Table 5. Lipid Profile According to Abdominal Obesity

Parameter	Abdominal Obesity	No Obesity	p-value
TC	208.0 ± 44.05	174.91 ± 35.31	0.003
HDL-C	59.98 ± 12.04	52.18 ± 10.12	0.006
LDL-C	133.9 ± 34.51	109.64 ± 27.27	0.005
TG	127.4 ± 78.81	120.77 ± 88.65	0.448

Abdominal obesity was defined according to waist circumference criteria (men >94 cm, women >80 cm). Values are presented as mean ± standard deviation.

Table 6. Lipid Profile According to BMI Status

Parameter	Overweight	Normal weight	p-value
TC	210.82 ± 43.82	181.94 ± 39.52	0.005
HDL-C	58.61 ± 11.3	56.25 ± 12.78	0.213
LDL-C	135.79 ± 34.09	115.09 ± 31.16	0.011
TG	140.18 ± 86.26	107.78 ± 72.75	0.060

Overweight defined as BMI >25 kg/m². BMI: Body Mass Index; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol.

Table 7. Metabolic Parameters According to Disease-Modifying Therapy

Parameter	Fingolimod	Ocrelizumab	Dimethyl fumarate	p-value
HOMA-IR	1.8 ± 0.88	1.71 ± 1.27	1.34 ± 0.61	0.271
TC	196.43 ± 46.61	202.07 ± 45.77	182.2 ± 35.7	0.552
HDL-C	57.93 ± 13.17	59.36 ± 13.35	60.7 ± 8.86	0.559
LDL-C	123.9 ± 36.69	129.2 ± 34.21	112.2 ± 26.97	0.388
TG	145.03 ± 92.37	119.29 ± 72.42	68.1 ± 16.81	0.020

FIN: Fingolimod; OCZ: Ocrelizumab; DMF: Dimethyl fumarate. Values are presented as mean ± standard deviation.

Table 8. Multivariate Regression Analysis for Predictors of EDSS

Variable	B	Std Error	Beta	p-value
Age	0.021	0.012	0.18	0.081
Disease duration	0.067	0.021	0.36	0.002
BMI	0.018	0.015	0.11	0.238
Waist circumference	0.012	0.009	0.13	0.176
LDL-C	0.004	0.003	0.10	0.214
Triglyceride	0.001	0.001	0.07	0.331
HOMA-IR	0.052	0.041	0.09	0.206

Dependent variable: EDSS (Expanded Disability Status Scale). B: unstandardized coefficient; Beta: standardized coefficient. Independent variables included age, disease duration, BMI, waist circumference, lipid parameters, and HOMA-IR.

DISCUSSION

The present study evaluated metabolic characteristics in patients with RRMS and explored their relationship with clinical disability. The findings demonstrate that MS patients exhibit increased adiposity and altered lipid profiles compared with healthy individuals.

One of the principal observations of this study is the higher prevalence of increased BMI and abdominal obesity among MS patients. Adiposity has been increasingly recognized as an important risk factor for MS development and progression. Adipose tissue secretes pro-inflammatory cytokines and adipokines that may contribute to systemic inflammation and immune dysregulation.

Despite the increased adiposity observed in MS patients, insulin resistance parameters were not significantly different between patients and controls. These findings are consistent with several previous studies suggesting that insulin resistance may be more strongly associated with obesity rather than MS itself.

The present study also demonstrated significant differences in lipid profile parameters between MS patients and healthy individuals. Elevated total cholesterol and HDL-cholesterol levels were observed in the patient group. Furthermore, patients with abdominal obesity and higher BMI showed significantly elevated total cholesterol and LDL-cholesterol levels.

Interestingly, no independent association was observed between lipid profile abnormalities and disability measured by EDSS. While some studies have reported correlations between lipid parameters and disease severity, others have failed to demonstrate such relationships. Differences in patient populations, disease duration, and methodological approaches may account for these discrepancies.

Another notable finding of this study was the lower triglyceride levels observed in patients receiving dimethyl fumarate therapy. Although the underlying mechanisms remain unclear, previous studies have suggested that certain disease-modifying therapies may influence lipid metabolism.

The results of this study suggest that metabolic alterations observed in RRMS may be primarily driven by adiposity rather than insulin resistance itself. These findings highlight the importance of monitoring metabolic health in patients with MS.

LIMITATIONS

This study has several limitations. First, the relatively small sample size may limit statistical power. Second, insulin resistance was assessed using HOMA-IR rather than more direct methods such as oral glucose tolerance testing or hyperinsulinemic clamp techniques. Finally, the cross-sectional design does not allow conclusions regarding causal relationships between metabolic alterations and disease progression.

CONCLUSION

Patients with RRMS demonstrate increased adiposity and alterations in lipid metabolism compared with healthy individuals. These metabolic changes appear to be more closely associated with body composition than with insulin resistance. Although lipid abnormalities were not independently

associated with neurological disability in this cohort, metabolic disturbances may represent important comorbid conditions that could influence long-term outcomes in MS.

Future prospective studies involving larger patient populations are required to further clarify the role of metabolic factors in MS pathophysiology and progression.

Declarations

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

FUNDING

This research received no external funding.

Author Contribution

Study design: Aylin Akçalı, Elif İşbilenData collection and analysis: Burak Akpek, Aylin AkçalıManuscript preparation: Burak AkpekAll authors approved the final version of the manuscript.

Data Availability

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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