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ORIGINAL ARTICLE

Gender-Specific Lipid Parameters Predict Excessive Daytime Sleepiness in Parkinson's Disease

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ABSTRACT

Background: **Lipid metabolism plays an important role in neurodegenerative diseases, including Parkinson's disease (PD). However, the relationship between lipid profiles and excessive daytime sleepiness (EDS) remains unclear. This study aimed to explore the relationship between lipid parameters and EDS in PD patients, especially focusing on gender differences.**
Methods: **A total of 176 PD patients were included in this study, and clinical data was collected. The Epworth Sleepiness Scale (ESS) was used to classify patients into PD EDS (ESS ≥ 8) and PD non-EDS (ESS < 8) groups. Univariate and multivariate analyses, along with receiver operating characteristic (ROC) analyses, were performed to detect potential biomarkers for EDS in PD.**
Results: **In male PD patients, univariate analysis indicated an association between disease duration, Hoehn-Yahr (H-Y) stage, and lipid parameters (total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C)) and EDS. Multivariate analysis identified TC and HDL-C as significant predictors, especially HDL-C. The TC/HDL-C ratio (AUC = 0.745) and non-HDL-C (defined as TC - HDL-C, AUC = 0.691) exhibited high predictive ability for EDS. Female PD patients, in contrast, showed no significant link between lipid parameters and EDS. Instead, motor dysfunction (UPDRS score) and psychological factors (HAMD/HAMA scores) were the main predictors of EDS in females.**
Conclusions: **Research findings indicate a significant gender difference in the factors influencing EDS in PD patients. In male PD patients, lipid metabolism disorders (elevated TC, reduced HDL-C) predict EDS, with TC/HDL-C and non-HDL-C as potential biomarkers. In female PD patients, motor and psychological factors primarily contribute to the risk of EDS.**
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KEYWORDS

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INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disorder worldwide, and the incidence is steadily increasing with age [1]. Excessive daytime sleepiness (EDS) is a debilitating non-motor symptom of PD. It increases the risks of patient accidents, cognitive decline, and psychological comorbidities such as depression and anxiety [2]. Despite its clinical signi-

ficance, the pathophysiological mechanisms underlying EDS in PD are poorly understood; therefore, an in-depth investigation is essential.

Emerging evidence suggests that lipid profiles correlate with PD progression. Reduced total cholesterol (TC) and HDL-C levels have been found to be associated with accelerated motor decline, whereas cognitive impairment is associated with elevated triglycerides (TG) [3]. However, studies on the interplay between lipid parameters and EDS have not been conclusive. Recent research findings indicate that neuroinflammation triggered by lipids may potentially disrupt the orexinergic neurons responsible for wakefulness in the lateral hypothalamus. This brain region is implicated in both PD and the regulation of sleep [4].

The gender differences in PD are also well studied. Males always have an earlier disease onset and a higher prevalence of sleep-disordered breathing, while females have greater motor symptom fluctuations in advanced stages and higher rates of mood disorders [5]. In comparison with age-matched people, pre-menopausal females tend to have higher levels of high-density lipoprotein cholesterol (HDL-C) and lower levels of low-density lipoprotein cholesterol (LDL-C). This advantage attenuates after menopause [6]. Lipid dysregulation affects neuronal membrane integrity, synaptic plasticity, and neuroinflammatory response in neurodegenerative diseases [7]. The impairment of cholesterol efflux from astrocytes caused by altered HDL-C exacerbates α-synuclein aggregation, whereas elevated LDL-C levels lead to oxidative stress and cause disruption of the blood-brain barrier [8]. The sex hormones modulate lipid metabolism and exert neuroprotective effects and may have a differential impact on EDS susceptibility in males and females [9].

This study explored gender-stratified relationships of lipid profiles (TC, TG, LDL-C, HDL-C) with EDS in PD. Our findings may provide insights for understanding EDS pathogenesis and guide targeted interventions to improve the quality of life in PD patients.

MATERIALS AND METHODS

Study subject selection and evaluation

The study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Soochow University (approval number: JD-LK-2018-061-01). From October 2022 through March 2024, PD patients admitted to the Neurology Department of the Second Affiliated Hospital of Soochow University were enrolled. They were between 30 and 80 years old. The inclusion criteria were meeting the 2015 PD diagnostic criteria established by the International Parkinson and Movement Disorder Society. The patients' data were collected by neurologists using multiple scales. The Epworth Sleepiness Scale (ESS) measured excessive daytime sleepiness, and disease severity was assessed by the Hoehn-Yahr (HY) staging [10]. The patients' motor function was evaluated by the Unified Parkinson's Disease Rating Scale (UPDRS) and its motor sub-scale (UPDRSIII). Sleep quality was assessed by the Pittsburgh Sleep Quality Index (PSQI) [11]. Cognitive function was assessed by the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) [12]. The Hamilton Depression Scale (HAMD) and Hamilton Anxiety Scale (HAMA) measured the patients' mental conditions. The Fatigue Severity Scale (FSS) evaluated the patients' tiredness. The patients who had taken sleeping, sedative effect, antidepressant, or anxiolytic drugs, or had an unclear medication history were excluded from the study. Patients who had serious comorbidities, including severe heart or brain diseases, cancer, or a head-trauma history were also excluded from the study.

Study design and grouping

The PD patients were grouped into PD-EDS and PD-nEDS groups according to ESS scores. Patients with ESS ≥ 8 were classified as EDS-positive (PD-EDS), and those with ESS < 8 as EDS-negative (PD-nEDS). Given the known influence of quality of nighttime sleep on EDS, the Pittsburgh Sleep Quality Index (PSQI) was also utilized. PSQI scores were added as covariates in regression models to control for variables that could bias the results. For each patient, the research team recorded age, gender, height, and weight to calculate the body mass index (BMI).

The laboratory technicians collected fasting venous blood samples to analyze lipid parameters: TC, TG, LDL-C, and HDL-C. For TC (CHOD-PAP) and TG (GPO-PAP), the serum was used after centrifugation. For HDL-C and LDL-C, heparin-anticoagulated plasma was used, then measured by direct homogeneous assays. To further enhance the analysis, non-traditional lipid parameters were calculated, including the TC/HDL-C ratio and non-HDL-C (TC minus HDL-C) [13]. Due to the well-established gender differences in PD and lipid metabolism, gender-stratified analyses were conducted. At the same time, 138 age and gender-matched individuals from the same hospital's physical exams formed the control group.

Statistical analysis

For continuous variables (lipid parameters, age, etc.), descriptive statistics like means, standard deviations, or medians and interquartile ranges were calculated. For the case of normally-distributed variables with homogeneous variances, independent-sample *t*-tests were used to compare two groups, one-way ANOVA was used for multiple-group comparisons. Non-parametric tests were used when data did not meet these criteria. F/H values denote the test statistics. For categorical variables, the chi-squared test was used to analyze group differences. Logistic regression identified risk factors for PD with EDS. Only variables demonstrating statistical significance in univariate analysis were retained for the multivariate logistic regression model. The receiver operating

Table 1. Comparison of clinical characteristics between PD patients and control groups.

Clinical parameter	PD group (n = 176)	Control group (n = 138)	t/χ^2 value	p-value
Gender				
Female	85(48.3)	53 (38.4)	3.071	0.080
Male	91 (51.7)	85 (61.6)		
Age (years)	63.22 ±9.08	62.52 ±8.91	0.684	0.495
Lipid parameters				
TC (mmol/L)	4.57 ± 0.93	4.99 ± 1.00	3.912	< 0.001
TG (mmol/L)	1.33 ± 0.94	1.63 ± 1.34	2.307	0.022
LDL-C (mmol/L)	2.68 ± 0.86	2.97 ± 0.88	2.880	0.004
HDL-C (mmol/L)	1.35 ± 0.36	1.33 ± 0.46	0.441	0.660
Non-HDL-C (mmol/L)	3.23 ± 0.88	3.67 ± 0.96	4.142	< 0.001

PD: Parkinson's disease, TC: total cholesterol, TG: triglycerides, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol. Data are presented as n (%), median (interquartile range), or mean ± SD.

Table 2. Comparison of clinical features between PD patients with and without EDS.

Clinical parameter	PD-EDS group (n = 65)	PD-nEDS group (n = 111)	t/χ^2 value	p-value
Gender				
Female	29 (44.6)	56 (50.5)	0.559	0.455
Male	36 (55.4)	55 (49.5)		
Age (years)	65.28 ± 8.34	62.02 ± 9.31	2.328	0.021
Education (years)	6.88 ± 4.68	7.41 ± 4.65	0.726	0.469
Disease duration (months)	81.43 ± 57.31	53.64 ± 47.81	3.295	0.001
HY stage	2.68 ± 0.91	2.20 ± 0.77	3.673	<0.001
UPDRS Total	54.55 ± 25.40	40.40 ± 20.08	3.845	<0.001
UPDRSIII (motor)	34.11 ± 16.83	27.08 ± 13.00	2.898	0.005
PSQI	10.17 ± 4.75	8.37 ± 4.65	2.442	0.016
MMSE	25.31 ± 4.01	25.79 ± 3.35	0.849	0.397
MoCA	20.20 ± 6.35	20.62 ± 5.73	0.443	0.658
HAMD	13.48 ± 8.44	10.47 ± 8.64	2.237	0.027
HAMA	12.44 ± 8.38	8.05 ± 6.61	3.821	<0.001
FSS	40.91 ± 15.33	34.35 ± 16.92	2.552	0.012
BMI	23.43 ± 3.17	23.41 ± 2.84	0.054	0.957
Lipid parameters				
TC (mmol/L)	4.69 ± 0.94	4.49 ± 0.91	1.414	0.159
TG (mmol/L)	1.48 ± 1.11	1.24 ± 0.81	1.616	0.108
LDL-C (mmol/L)	2.79 ± 0.86	2.62 ± 0.85	1.216	0.226
HDL-C (mmol/L)	1.29 ± 0.37	1.38 ± 0.36	1.571	0.118
Non-HDL-C (mmol/L)	3.41 ± 0.89	3.12 ± 0.86	2.079	0.039

PD-EDS: Parkinson's disease with excessive daytime sleepiness, PD-nEDS: Parkinson's disease without excessive daytime sleepiness, UPDRS: Unified Parkinson's Disease Rating Scale, PSQI: Pittsburgh Sleep Quality Index, MMSE: Mini-Mental State Examination, MoCA: Montreal Cognitive Assessment, HAMD: Hamilton Depression Scale, HAMA: Hamilton Anxiety Scale, FSS: Fatigue Severity Scale, BMI: body mass index. Data are presented as n (%), median (interquartile range), or mean ± SD.

Table 3. Gender-stratified lipid profiles in PD patients and controls.

Lipid parameter	PD-Male (n = 91)	PD-Female (n = 85)	Control-Male (n = 85)	Control-Female (n = 53)	F/H Value	p-value
TC (mmol/L)	4.27 ± 0.76	4.89 ± 0.98	5.03 ± 1.10	4.94 ± 0.82	11.892	< 0.001
TG (mmol/L)	1.30 ± 1.06	1.36 ± 0.79	1.74 ± 1.57	1.45 ± 0.83	2.481	0.061
LDL-C (mmol/L)	2.42 ± 0.73	2.97 ± 0.90	3.01 ± 0.98	2.90 ± 0.68	25.280	< 0.001
HDL-C (mmol/L)	1.26 ± 0.34	1.44 ± 0.36	1.28 ± 0.52	1.39 ± 0.35	3.785	0.011
Non-HDL-C (mmol/L)	3.43 ± 0.94	3.47 ± 0.99	3.02 ± 0.71	3.54 ± 0.79	29.558	< 0.001

TC: total cholesterol, TG: triglycerides, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol. Data are presented as mean ± SD.

Table 4. Univariate and multivariate logistic regression analysis of EDS risk factors in female PD patients.

Clinical parameter	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Disease duration (months)	1.011 (1.003 - 1.019)	0.009	0.997 (0.983 - 1.012)	0.685
HY stage	2.075 (1.244 - 3.461)	0.005	0.569 (0.205 - 1.580)	0.569
UPDRS total	1.037 (1.016 - 1.058)	0.001	1.147 (1.025 - 1.284)	0.017
UPDRSIII (motor)	1.051 (1.019 - 1.084)	0.002	0.887 (0.780 - 1.010)	0.070
PSQI	1.027 (0.938 - 1.124)	0.568		
HAMD	1.054 (1.001 - 1.111)	0.047	0.873 (0.770 - 0.989)	0.033
HAMA	1.103 (1.033 - 1.178)	0.003	1.143 (1.013 - 1.290)	0.030
FSS	1.026 (0.996 - 1.056)	0.089		
TC (mmol/L)	1.132 (0.712 - 1.798)	0.600		
TG (mmol/L)	1.249 (0.714 - 2.187)	0.436		
LDL-C (mmol/L)	1.065 (0.636 - 1.784)	0.811		
HDL-C (mmol/L)	1.029 (0.283 - 3.735)	0.965		

OR: odds ratio, CI: confidence interval.

Table 5. Univariate and multivariate logistic regression analysis of EDS risk factors in male PD patients.

Clinical parameter	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Disease duration (months)	1.010 (1.001 - 1.020)	0.035	1.005 (0.994 - 1.016)	0.375
HY stage	1.854 (1.009 - 3.404)	0.047	1.671 (0.771 - 3.622)	0.193
UPDRS total	1.017 (0.996 - 1.039)	0.106		
UPDRSIII (motor)	1.013 (0.982 - 1.045)	0.404		
PSQI	1.159 (1.043 - 1.289)	0.006	1.087 (0.961 - 1.229)	0.184
HAMD	1.032 (0.980 - 1.086)	0.237		
HAMA	1.070 (1.003 - 1.141)	0.041	1.062 (0.979 - 1.152)	0.146
FSS	1.026 (0.998 - 1.055)	0.068		
TC (mmol/L)	1.911 (1.041 - 3.506)	0.037	3.107 (1.016 - 9.505)	0.047
TG (mmol/L)	1.381 (0.845 - 2.258)	0.198		
LDL-C (mmol/L)	1.998 (1.008 - 3.960)	0.047	1.042 (0.375 - 2.893)	0.937
HDL-C (mmol/L)	0.242 (0.059 - 0.988)	0.048	0.062 (0.007 - 0.527)	0.011

OR: odds ratio, CI: confidence interval.

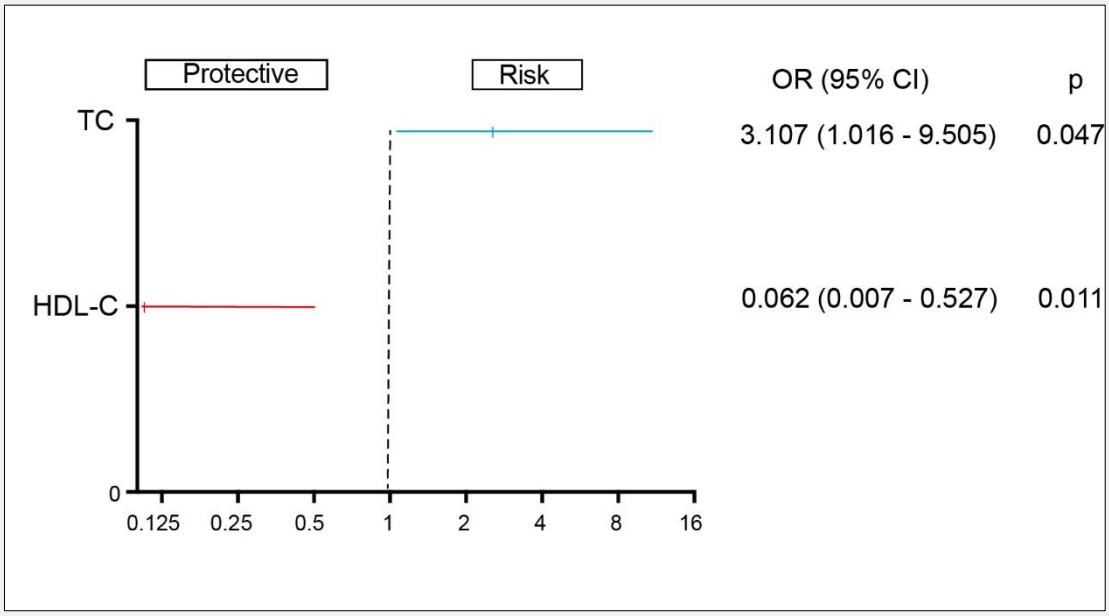

Figure 1. Analysis of risk factors for male PD patients.

OR = 0.062 < 1: HDL-C was a protective factor in male PD, OR = 3.107 > 1: TC was a risk factor.

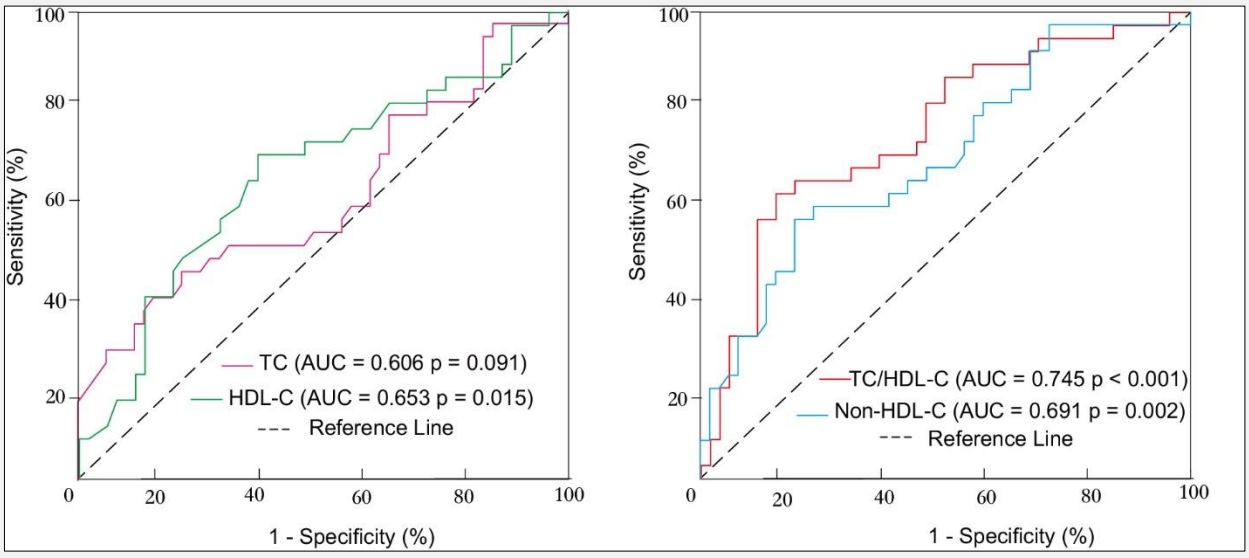

Figure 2. ROC analysis of lipid parameters for predicting EDS in male PD patients.

characteristic (ROC) curve analysis evaluated the predictive power of clinical data. The area under the curve (AUC), 95% confidence interval, optimal cutoff value, sensitivity, and specificity were also calculated. A two-sided test with a significance level of 0.05 was adapted, and $p < 0.05$ was considered statistically significant. Analyses were carried out using SPSS 24.0 (IBM Corp., Armonk, NY, USA, version 24.0), GraphPad 7.0e (GraphPad Software, San Diego, CA, USA, version 7.0e), and Adobe Illustrator 2022 (Adobe Inc., San Jose, CA, USA, version 26).

RESULTS

Clinical characteristics of PD patients versus controls

A total of 176 PD patients and 138 controls were enrolled. No significant differences were observed in gender ratio (male: 51.7% vs. 61.6%, $p = 0.080$) or average age (63.22 vs. 62.52 years old, $p = 0.495$) between the two groups. PD patients exhibited lower levels of TC (4.57 vs. 4.99 mmol/L, $p < 0.001$), TG (1.33 vs. 1.63 mmol/L, $p = 0.022$), LDL-C (2.68 vs. 2.97 mmol/L, $p = 0.004$), and non-HDL-C (3.23 vs. 3.67 mmol/L, $p < 0.001$), while HDL-C remained comparable (1.35 vs. 1.33 mmol/L, $p = 0.660$) (Table 1).

Clinical characteristics of PD patients with and without EDS

Among all PD patients, 65 individuals (accounting for 36.9%) were classified as EDS-positive (ESS ≥ 8). PD-EDS patients were older in age (average age: 65.28 vs. 62.02 years, $p = 0.021$), had longer disease duration (81.43 vs. 53.64 months, $p = 0.001$), and had higher Hoehn-Yahr (H-Y) staging (2.68 vs. 2.20, $p < 0.001$) compared to PD-nEDS patients. PD-EDS patients exhibited significantly poorer sleep quality during the night (PSQI: 10.17 vs. 8.37, $p = 0.016$) compared to PD-nEDS patients. Motor disorder (UPDRS total score: 54.55 vs. 40.40, $p < 0.001$) and psychological distress (HAMD: 13.48 vs. 10.47, $p = 0.027$; HAMA: 12.44 vs. 8.05, $p < 0.001$) were higher in the EDS group. Across all subgroups, no lipid parameters (TC, TG, LDL-C, HDL-C) showed significant differences, except for non-HDL-C ($p = 0.039$) (Table 2).

Gender-specific comparisons of PD clinical characteristics

Male PD patients achieved higher education levels than females. Their disease duration and motor scores (UPDRS, HY staging) were comparable to those of females (all $p > 0.05$). Female PD patients showed poorer cognitive performance (MMSE: 24.46 vs. 26.68, $p < 0.001$; MoCA: 18.67 vs. 22.12, $p < 0.001$).

Female PD patients exhibited higher psychological distress (HAMD: 12.39 vs. 10.85, $p = 0.243$; HAMA: 10.33 vs. 8.99, $p = 0.244$), but these differences were statistically nonsignificant (Supplementary Table 1). Gender-stratified comparisons showed significant differences in lipid parameters between PD patients and controls. Male PD patients demonstrated lower TC, LDL-C, and HDL-C levels when compared with male controls and female PD patients ($p < 0.05$). The overall difference in TG was nonsignificant (Table 3, Supplementary Figure).

Gender-dependent risk factors for EDS in PD

In female PD patients, univariate logistic regression analysis identified several significant risk factors for EDS, including disease duration (OR = 1.011, 95% CI: 1.003 - 1.019, $p = 0.009$), H-Y stage (OR = 2.075, 95% CI: 1.244 - 3.461, $p = 0.005$), UPDRS total score (OR = 1.037, 95% CI: 1.016 - 1.058, $p = 0.001$), UPDRS III motor score (OR = 1.051, 95% CI: 1.019 - 1.084, $p = 0.002$), HAMD (OR = 1.054, 95% CI: 1.001 - 1.111, $p = 0.047$), and HAMA (OR = 1.103, 95% CI: 1.033 - 1.178, $p = 0.003$). Lipid parameters showed no association with EDS (all $p > 0.05$). Multivariate logistic regression analysis demonstrated motor severity (UPDRS total: OR = 1.147, 95% CI: 1.025 - 1.284, $p = 0.017$) and psychological factors, depression (HAMD: OR = 0.873, 95% CI: 0.770 - 0.989, $p = 0.033$) and anxiety (HAMA: OR = 1.143, 95% CI: 1.013 - 1.290, $p = 0.030$), were key predictors (Table 4).

In male PD patients, univariate logistic regression analysis identified several significant risk factors for EDS, including disease duration (OR = 1.010, 95% CI: 1.001 - 1.020, $p = 0.035$), H-Y stage (OR = 1.854, 95% CI: 1.009 - 3.404, $p = 0.047$), TC (OR = 1.911, 95% CI: 1.041 - 3.506, $p = 0.037$), LDL-C (OR = 1.998, 95% CI: 1.008 - 3.960, $p = 0.047$), and HDL-C (OR = 0.242, 95% CI: 0.059 - 0.988, $p = 0.048$). Multivariate logistic regression analysis, adjusted for PSQI scores, showed that lipid parameters retained independent predictive value for EDS. TC (OR = 3.107, 95% CI: 1.016 - 9.505, $p = 0.047$) and HDL-C (OR = 0.062, 95% CI: 0.007 - 0.527, $p = 0.011$) were identified as independent predictors of EDS (Table 5, Figure 1).

Predictive value of lipid parameters for EDS in male PD patients

Non-traditional lipid parameters (TC/HDL-C and non-HDL-C) were chosen for ROC analysis because they are known to be useful as combined markers for both heart disease risk and brain health issues. This decision was also supported by earlier results showing that TC and HDL-C can independently predict EDS. ROC analysis revealed that both the TC/HDL-C ratio (AUC = 0.745, 95% CI: 0.638 - 0.851, $p < 0.001$) and non-HDL-C (AUC = 0.691, 95% CI: 0.578 - 0.804, $p = 0.002$) exhibited strong predictive value for identifying EDS risk in male PD patients. TC alone exhibited moderate predictive performance (AUC = 0.606, 95% CI: 0.482 - 0.731, $p = 0.091$), while HDL-C (AUC = 0.653, 95% CI: 0.534 - 0.772, $p = 0.015$) also achieved statistical significance (Supplementary Table 2, Figure 2).

DISCUSSION

This study explored the clinical implications of gender differences in the pathogenesis of EDS among PD patients. While high TC and low HDL-C was identified as a critical biomarker for EDS in male PD patients, no significant lipid-EDS associations were observed in their female counterparts. Instead, motor dysfunction and psychological distress proved to be the major factors contributing to EDS in females.

In male PD patients, dysregulated lipid metabolism emerged as a key predictor of EDS. Elevated TC and reduced HDL-C were independently associated with increased EDS risk. These findings corroborate evidence that associates cholesterol metabolism with both neurodegenerative mechanisms and the regulation of sleep-wake cycles [14]. HDL-C protects brain cells through its anti-inflammatory and antioxidant actions, potentially safeguarding sleep-control areas in the brainstem and hypothalamus from damage. Elevated cholesterol levels impair blood-brain barrier integrity and facilitate α-synuclein fibril formation; pathological processes that may exacerbate both PD neurodegeneration and sleep-wake cycle dysregulation [15]. For this reason, gender-specific predictive models incorporating TC/HDL-C and non-HDL-C ratios could enhance personalized management strategies for male PD patients. By tracking these lipid indices, clinicians can proactively identify at-risk male patients, facilitating timely initiation of evidence-based interventions including statin therapy and personalized lifestyle counseling.

The little association between lipid profiles and EDS in females indicate potential hormonal or metabolic modifiers that warrant targeted investigation. Estrogen controls fat processing and safeguards neural tissue, potentially accounting for the absent lipid-EDS link in females, and may mitigate lipid-mediated neurotoxicity in premenopausal women [16]. Although the female cohort in our study had an average age exceeding 60 years (likely postmenopausal status), lipid parameters demonstrated no predictive value for EDS. This observation goes against what we would predict, as the estrogen reduction following menopause typically leads to poorer lipid metabolism. One possible explanation could be that estrogen's protective effects on the nervous system might endure past menopausal estrogen decline. Another possibility is that female-specific factors, particularly body fat distribution, may play a greater role than lipid levels. Gender-specific fat distribution patterns show differential risks: male-dominant visceral adiposity (fat around organs) correlates with pro-inflammatory states and neurodegeneration, while female subcutaneous deposition (fat under the skin) may confer alternative metabolic consequences [17]. In fact, motor impairment (measured by UPDRS III) and psychological symptoms (measured by HAMD/HAMA) were identified as the predominant risk factors for EDS. These findings are consistent with epidemiological data indicating female PD patients experience greater PD-related disability and higher rates of mood disorders [18]. We should recognize the critical importance of comprehensive care that addresses both motor impairment and psychological distress in this population [19].

There are limitations in this investigation due to its retrospective cross-sectional design, which restricts causal inference. While the sample size was sufficient for gender-based stratification, it limited more detailed analyses by PD subtypes and progression stages. Potential unmeasured confounders, including dietary habits, statin use, genetic factors, and comorbid cardiovascular conditions were not systematically assessed. These may have influenced the results. In the future, our research will employ multi-omics approaches (such as lipidomics, proteomics) to pinpoint specific lipid profiles and inflammatory biomarkers associated with EDS development. Combining lipoprotein(a), white matter imaging (DTI), brain network scans (fMRI), and transcranial stimulation with EEG could reveal how lipids affect sleep-control circuits.

CONCLUSION

We observed significant gender-specific differences in EDS prevalence among PD patients. In male patients, lipid homeostasis represents a clinically modifiable risk factor for EDS. Routine cholesterol monitoring and targeted lipid-modifying therapies may represent actionable strategies to mitigate EDS risk in this population. In female patients, motor impairment and psychological distress are primary concerns, requiring combined movement disorder and mental health management rather than cholesterol-focused therapies. These results enable the creation of personalized approaches to combat sleep disturbances in neurodegeneration.

Declaration of Interest:
The authors declare no conflict of interest.

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