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Association between normal weight obesity and lipids profile in Slovak women aged 38 to 59 years

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Abstract: Obesity and its associated health problems are an issue, especially when weight gain is not outwardly visible. Individuals with the same Body Mass Index (BMI) may differ in body fat percentage and may unknowingly suffer from normal weight obesity (NWO). Middle-aged women are at high risk if their body composition changes due to factors such as age, health status or reproductive history. This study investigated the relationship between NWO and lipid profile in middle-aged women. A sample of 122 women aged 38 to 59 years (47.17 ± 5.24) from Slovakia participated in this study. Using a questionnaire, participants answered questions about lifestyle, health background, sociodemographic classification, reproductive and menstrual history. The anthropometric parameters were determined using standard methods. Body composition was measured using a bioelectrical impedance analyzer. Biochemical parameters were determined from morning blood samples. Blood pressure was assessed in a sitting position using a digital sphygmomanometer. The primary aim of this study was to assess the differences in lipid profiles between NOW women and normal weight-lean (NWL) women. Our results showed statistically significantly higher values of uric acid in the women with NWO compared to NWL women (237.39 ± 54.11 μmol/l vs. 213.02 ± 52.64 μmol/l; $p = 0.009$). Moreover, significant differences were noted between NWO women and NWL women in body height, body weight, waist and hip circumference, WHR, BMI and fat mass (%, $p < 0.05$). Other biochemical variables showed no statistically significant differences between the study groups of women. Elevated uric acid levels in women diagnosed with NWO may serve as an indication of metabolic imbalance associated with undetected obesity. These results underscore the importance of implementing early detection and intervention methods for NWO to prevent related health issues. Further research is necessary to investigate the underlying factors contributing to these connections and evaluate the efficacy of customized interventions.

Key Words: excessive fat mass, lipids, BMI, middle age.

Original article

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Introduction

Weight gain is one of the biggest health problems in midlife. The changes in the body in midlife are due to many factors, such as age, health status, gender, genetic predisposition, and reproductive history. These changes can be assessed using anthropometric measures such as Body Mass Index (BMI), bioelectrical impedance analysis (BIA), or biochemical assessments (Luptáková et al. 2013a; Drozdová et al. 2016; Danková et al. 2017; Falbová et al. 2019, 2020, 2022a; Vorobeľová et al. 2021, 2023; Hurtado et al. 2024).

In recent decades, the global increase in obesity rates has been closely linked to a rising risk of chronic diseases such as diabetes, cardiovascular disease, and dyslipidemia (Fruh et al. 2017; Welsh et al. 2024). The World Health Organization (WHO) defines obesity as an excessive accumulation of fat that poses a health risk; this emphasizes the importance of considering not only Body Mass Index (BMI), a common measure used to classify overweight and obesity, but also fat mass (FM) to understand the complexity of the disease. Studies show that lean and obese individuals have different metabolic profiles, emphasizing the need to measure fat mass to gain a comprehensive understanding of obesity-related disease trajectories (Hirsch et al. 2016; Bosy-Westphal et al. 2021). In addition, participants with identical BMI may differ in terms of body fat percentage (BFP) and FM distribution, further highlighting the nuanced nature of obesity (Cota et al. 2021). The concept of normal weight obesity (NWO), first described by DeLorenzo in 2006 has emerged to address this phenomenon. This phenotype characterizes individuals with a BMI that indicates a normal weight (BMI < 25 kg/m^2) but who have excess FM (FM > 30%). Despite being of normal weight, individuals classified as NWO have a similar risk of cardiovascular disease, type 2 diabetes, and metabolic syndrome as overweight and obese individuals (Cota et al. 2021; Ashtary-Larky et al. 2023). The discrepancy between BMI and the assessment of health risks arises due to the fact that BMI does not consider the distribution and percentage of body fat, which are crucial elements in determining an individual's overall health. As a result, individuals with NWO may not be identified as at-risk based on BMI alone, leading to a lack of appropriate interventions and an increased risk of health complications.

In addition, estradiol induces vasoprotective effects via multiple mechanisms, including alterations in plasma concentrations of lipoproteins (decrease in low-density lipoprotein cholesterol (LDL-C) levels, reducing oxidized LDL formation, increasing high-density lipoprotein cholesterol levels (HDL-C), hemostatic factors, glucose, and insulin (Dubey and Jackson 2001). Estrogen deficiency in midlife after menopause is the main reason for the deterioration of serum lipid profiles (Rexrode et al. 2003; Luptáková et al. 2012; Fonseca et al. 2017; Vorobeľová et al. 2019; Falbová et al. 2022b).

In this cross-sectional study, we attempted to clarify the association between NWO and lipids profile in middle-aged Slovakian women, due to the limited number of studies available in the literature on the topic and since the effect of increased of fat mass on lipid, inflammation or glycaemic status remains to be verified (Marques-Vidal et al. 2010).

Material and methods

Participants

This study was based on data collected from a cross-sectional survey in Slovakia. The women were recruited from various locations in Slovakia's west, south, and center (51.9% were born in towns), through an invitation letter, which was distributed prior to data collection with the aid of local physicians. The women were approached and recruited using a non-random procedure based on voluntariness and convenience. The studied sample consisted of 122 middle-aged women, aged between 38 and 59 years, with an average age of 47.17 ± 5.24 years. All women were interviewed at a medical examination facility in the morning and assessed for medical, anthropometric, and lifestyle factors at local health centers. Each woman provided written informed consent for this study-following the principles of the Declaration of Helsinki. Those who were unable to give a response due to severe physical or mental illness and on whom anthropometry and blood measurements could not be performed were excluded from the study. The women were divided into two groups according to their BMI and FM (%) – NWO women (BMI < 25 kg/m^2, FM > 30%) and normal weight lean (NWL) women (BMI < 25 kg/m^2, FM < 30%).

Questionnaire

The women were interviewed using pre-tested questionnaires on their reproductive and menstrual history, socio-demographic background, lifestyle, and health status designed by Kaczmarek (Kaczmarek 2007) and validated in Polish studies (The Menopause-Specific Questionnaire, A. Mickiewicz University Poznań, Poland, Maria Kaczmarek). All socio-demographic and lifestyle variables were self-reported. Smoking status was divided into current ‚smokers' (smoking once a week to daily) and non-smokers (never smoked). Physical activity was categorized into two groups: regular and never, including occasionally. Education was divided into three groups: basic, secondary, and university education.

Anthropometric analysis and body composition

Anthropometric measurements were taken after participants had removed their shoes and heavy clothing. Data were collected by trained anthropologists using standard Martin and Saller techniques. (1) height was measured to an accuracy of 0.5 cm using a Sieber and Hegner anthropometer at the head with the participant standing barefoot with the feet together; (2) body weight was measured on a personal weight scale to an accuracy of 0.1 kg; and (3) BMI was calculated as body weight divided by height squared. Waist and hip circumferences were measured according to the NHLBI Obesity Education Initiative (Audrain-McGovern and Benowitz 2011) and the WHO (2011). The WHR was calculated as the waist circumference divided by the hip circumference.

Body composition measurements were performed in the morning utilizing a bioelectrical impedance analyzer (BIA 101, Akern S.r.l.) at a signal frequency of 50 kHz, with a constant excitation current of 800 μA and a four-electrode arrangement. Bioimpedance is a complex measurement composed of resistance (R, ohm) related to the amount of fluid and reactance (XC, ohm) associated with the cell membrane's capacitance. This study determined the FM (%) using Bodygram (version 1.21, Akern S.r.l) program.

Biochemical analysis

Blood samples were collected in the morning after at least 12 hours of fasting. Biochemical values of bilirubin, glucose, gamma-glutamyltransferase (GGT), alanine aminotransferase (ALT), creatinine, uric acid (UA), total cholesterol (TC), HDL-cholesterol (HDL-C) and triglycerides (TG) were analyzed from fasting plasma samples using routine laboratory procedures at the Clinical Laboratories Department of Bratislava Alpha Medical. Low-density lipoprotein cholesterol (LDL-C) was calculated from the total cholesterol, HDL-C, and triglycerides values using the Friedewald equation when triglycerides were 4.5 mmol/L. LDL-C was considered as absent if the serum triglyceride concentration exceeded this threshold. The atherogenic indices were calculated as follows: AI1 = TC (mmol/L) / HDL-C (mmol/L), AI2 (non-HDL-C) = TC (mmol/L) – HDL-C (mmol/L), and AI3 = LDL-C (mmol/L) / HDL-C (mmol/L). The atherogenic index of plasma (AIP) was calculated as the logarithmically transformed ratio of the TG to HDL-C molar concentrations (mmol/l).

Blood pressure (BP) assessment

BP and pulse rate were measured in a sitting position using a digital sphygmomanometer (Omron M3). Each measurement was performed three times, and the average values for systolic blood pressure (mmHg; SBP), diastolic blood pressure (mmHg; DBP), and pulse rate (pulse/min) were then determined.

Statistical analysis

All statistical analyses were performed using IBM SPSS for Windows (Statistical Package for the Social Science, version 24.0, Chicago, IL), with statistical significance at $p \leq 0.05$. The obtained frequencies and percentages determined participants' responses, and the normality assumption hypothesis for continuous variables was tested by a one-sample Kolmogorov–Smirnov test. The differences between NWO and NWL women in the category variables were tested with Pearson Chi-square in contingency tables. The parametric Independent Samples T-Test and the non-parametric Mann-Whitney U test were used based on the normality distribution of the quantitative variables.

Results

Table 1 depicts the baseline characteristics of the women under study, divided into the NWL group, comprised 57 participants (age 46.56 ± 4.78 SD), and the NWO group (age 48.11 ± 5.46 SD), comprised 65 individuals. Statistically significant differences between the two groups were observed in the following variables: body height (cm; $p = 0.013$), body weight (kg; $p < 0.001$), waist circumference (cm; $p < 0.001$), hip circumference (cm; $p < 0.001$), BMI (kg/m^2; $p < 0.001$), WHR ($p = 0.015$) and FM (%; $p < 0.001$).

On the contrary, no differences were observed in the variables age (y; $p = 0.119$), SBP (mmHg; $p = 0.438$), and DBP (mmHg; $p = 0.577$). Overall, the NWO group presented higher values across all the mentioned variables except for body height (cm) and DBP (mmHg). Moreover, other factors such as smoking, sports activity, and education were reported across these two groups. Only 19 (33.34) women smoked in the NWL group, whereas 12 (18.46%) smoked in the NWO group ($p = 0.060$). In the NWL group, 18 (31.58%) performed regular sports activity, and 13 (20%) performed regular sports activity in the NWO group (p = 0.143). In regards to education, in the NWL group, 7 (12.28%) had a basic level, 41 (71.93%) had a secondary level, and 9 (15.79%) had a university degree; similarly, in the NWO group, 10 (15.38%) had a basic level of education, 46 (70.78%) secondary and 9 (13.84%) a university degree (p = 0.864).

Table 1. Baseline characteristics of the study women

	NWL	NWO	
Number of participants	N = 57 (46.72%)	N = 65 (53.28%)	
	Mean ± SD	**Mean ± SD**	***p***
Age, y	46.56 ± 4.78	48.11 ± 5.46	0.119
Body Height (cm)	165.35 ± 5.56	162.89 ± 5.18	0.013
Body Weight (kg)	57.83 ± 6.30	62.55 ± 4.65	<0.001
Waist circumference (cm)	70.35 ± 7.08	76.67 ± 6.43	<0.001
Hip circumference (cm)	93.18 ± 4.84	97.60 ± 4.32	<0.001
BMI (kg/m^2)	21.11 ± 1.65	23.55 ± 0.91	<0.001
WHR	0.75 ± 0.06	0.79 ± 0.07	0.015
Fat mass (%)	25.07 ± 4.37	32.88 ± 2.11	<0.001
SBP (mmHg)	116.05 ± 15.37	118.08 ± 15.28	0.438
DBP (mmHg)	75.79 ± 10.17	75.02 ± 9.10	0.577
	N (%)	**N (%)**	
Smoking status			***p***
Smokers	19 (33.34)	12 (18.46)	0.060
Non-smokers	38 (66.67)	53 (81.54)	
Regular sport activity			
Yes	18 (31.58)	13 (20.00)	0.143
No	39 (68.42)	52 (80.00)	
Education			
Basic	7 (12.28)	10 (15.38)	
Secondary	41 (71.93)	46 (70.78)	0.864
University	9 (15.79)	9 (13.84)	

Note: N, number of participants; p, value of statistical significance; SD, standard deviations; NWL, normal weight lean; NWO, normal weight obesity, SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, Body Mass Index; WHR, waist to hip ratio

Table 2 compares the mean values of selected biochemical variables and atherogenic indices between women with NWL and NWO. The primary objective of this study was to assess the variations in lipid profiles, which encompass Total Cholesterol (TC), Low-Density Lipoprotein Cholesterol (LDL-C), High-Density Lipoprotein Cholesterol (HDL-C), and Triglycerides (TG). The NWO group exhibited lower mean TC levels when contrasted with the NWL group. The mean TC for the NWO group amounted to 5.29 ± 0.95 mmol/L, whereas the NWL group displayed a mean TC of 5.42 ± 1.09 mmol/L (p = 0.592). Conversely, the NWL group had elevated LDL-C levels, with a mean of 3.19 ± 1.01 mmol/L, in contrast to the NWO group, which had a mean of 2.99 ± 0.86 mmol/L (p = 0.243). Additionally, the NWO group showed lower HDL-C levels, with a mean of 1.70 ± 0.50 mmol/L, compared to the NWL group, which had a mean of 1.79 ± 0.43 mmol/L (p = 0.299). The NWO group had higher TG levels, averaging 1.25 ± 1.07 mmol/L, whereas the NWL group averaged 0.98 ± 0.38 mmol/L (p = 0.065).

Table 2**.** Selected biochemical variables between NWL and NWO women

	NWL				NWO				
	N	Mean		SD	N	Mean		SD	*p*
Total cholesterol, (mmol/L)	57	5.42	±	1.09	65	5.29	±	0.95	0.592
Triglycerides, (mmol/L)	57	0.98	±	0.38	65	1.25	±	1.07	0.065
HDL-C, (mmol/L)	56	1.79	±	0.43	59	1.70	±	0.50	0.299
LDL-C, (mmol/L)	56	3.19	±	1.01	59	2.99	±	0.86	0.243
AI1 (TC/HDL-C)	56	3.16	±	0.90	59	3.28	±	1.18	0.946
AI2 (TC-HDL-C)	56	3.63	±	1.06	59	3.54	±	0.99	0.637
AI3 (LDL-HDL-C)	56	1.90	±	0.80	59	1.91	±	0.95	0.663
AIP log (TG/HDL-C)	56	-0.29	±	0.21	59	-0.21	±	0.28	0.115
Creatinine (μmol/L)	57	69.28	±	7.31	65	69.47	±	8.33	0.892
Bilirubin (μmol/L)	57	9.80	±	4.71	65	9.55	±	4.71	0.795
Glucose (mmol/L)	57	4.59	±	0.68	63	4.67	±	0.61	0.323
Gamma-glutamyltransferase (μkat/L)	57	0.29	±	0.18	65	0.29	±	0.17	0.898
Alanine aminotransferase (μkat/L)	57	0.25	±	0.08	65	0.29	±	0.20	0.736
Uric acid (μmol/L)	57	213.02	±	52.64	65	237.39	±	54.11	0.009
APO A1	56	1.77	±	0.27	59	1.76	±	0.29	0.972
ApoB/ApoA1	56	0.50	±	0.17	59	0.51	±	0.18	0.894

Abbreviations: N, number of participants; p, value of statistical significance; SD, standard deviations; NWL, normal weight lean; NWO, normal weight obesity; HDL-C, high-density lipoprotein – cholesterol; LDL-C, low-density lipoprotein-cholesterol; TC, total cholesterol; TG, triglycerides; AI, Atherogenic index; APO, apolipoprotein

The women with NWO achieved statistically significantly higher mean values of UA compared to women with NWL (237.39 ± 54.11 μmol/l vs. 213.02 ± 52.64 μmol/l). No statistically significant differences were found in other biochemical variables between the women's study groups.

Discussion

Our results show significant differences between the NWL and NWO groups in various anthropometric measures, such as body weight, waist circumference, hip circumference, BMI, WHR and FM (%). These findings suggest that despite both groups being classified as normal weight by BMI, there are significant differences in body composition and fat distribution, which emphasizes the importance of considering waist circumference as a marker of central obesity. The fact that no significant differences in age and blood pressure were found between the two groups suggests that these factors are unlikely to influence the differences in anthropometric measures. The insignificant variations in blood pressure levels suggest that both groups exhibit comparable cardiovascular profiles in terms of hypertension risk. This observation is significant because it implies that the metabolic disturbances observed in the NWO group, such as increased uric acid levels, may not necessarily be reflected in conventional cardiovascular risk markers, such as blood pressure. This emphasizes the importance of examining beyond traditional metrics to gain a comprehensive understanding of metabolic health, especially in individuals with normal body weight. We can see insights into lifestyle factors such as smoking habits, sports activity and education level between the two groups. Although not statistically significant, the differences in smoking, physical activity and education levels are worth noting as they might have had an impact on overall health and risk factors associated with body composition (Falbová et al. 2023) and obesity (Vorobeľová et al. 2022). Smoking is widely recognized as a significant contributor to a variety of health issues, such as cardiovascular disease and metabolic syndrome. It can increase insulin resistance and inflammation, thereby exacerbating metabolic health in individuals with NOW (Chiolero et al. 2008). The potential impact of smoking on metabolic health in NWO individuals warrants further investigation, as addressing smoking cessation could be a critical intervention for improving health outcomes in this population. Moreover, it is crucial to engage in regular physical activity in order to preserve metabolic health and prevent obesity-related diseases. Although the difference in reported physical activity levels was not considered statistically significant, even minor variations in physical activity can have significant implications for one's health (Petridou et al. 2019). Future studies should consider more precise measures of physical activity and their direct effects on metabolic parameters in NWO individuals. Education level is often correlated with health literacy, access to healthcare, and lifestyle choices. Although our study found no significant differences in education levels, higher education may be associated with better health outcomes due to increased awareness and adoption of healthier behaviors (Zajacova et al. 2018). The role of education in influencing health behaviors and metabolic health outcomes in NWO individuals is an area that deserves more detailed examination. Similarly, studies by Opoku et al. (2023) and Luptáková et al. (2013b) found significant associations between obesity, metabolic syndrome and various anthropometric measures such as body weight, waist circumference and BMI. Thus, the studies indicate that central obesity, as reflected by increased waist circumference, is associated with unfavorable metabolic outcomes regardless of BMI. The difference between the present study and the study by Opoku et al. (2023) is that the latter focuses more generally on obesity at different stages of menopause without considering NWO. In the present study, a significant difference in UA levels was found between the NWL and NWO groups, with significantly higher levels observed in the NWO group. Several mechanisms may explain the association between elevated UA levels and obesity. Excess body fat may be associated with increased UA production and impaired secretion due to insulin resistance, leading to impaired UA metabolism and even hyperuricemia (Kızılay et al. 2019; Li et al. 2021). Elevated UA levels can also contribute to obesity by stimulating hepatic and peripheral fat synthesis (Johnson et al. 2011). This increase in UA levels is associated with metabolic and cardiovascular disease, suggesting possible effects of central obesity on metabolic health in women. In a study by Taheri et al (2020), a significant negative association was found between adiponectin levels and lipid profiles in women with NWO. Lower adiponectin levels correlated with higher levels of total cholesterol, LDL cholesterol and triglycerides, suggesting a possible protective function of adiponectin against dyslipidemia in this population. In a long-term surveillance study of 2873 women conducted over 30 years, 574 women exhibited initial clinical symptoms of coronary heart disease (CHD). Metabolic risk factors, such as cholesterol, glucose tolerance, uric acid, and menopause, were found to be correlated with the development of CHD. The study revealed that serum total cholesterol was a significant predictor of CHD in both men and women. However, impaired glucose tolerance eliminated the female advantage in CHD risk. Central obesity poses a higher CHD risk for women, and the risk is two to three times higher for postmenopausal women than for premenopausal women, as per Kannel's research in 1987. Impaired glucose tolerance is a prevalent issue among obese individuals and often leads to insulin resistance and type 2 diabetes, as per Wondmkun's study in 2020. In obese patients, insulin resistance may also explain the connection between decreased bilirubin levels and increased body fat percentage. The activity of heme oxygenase-1, the enzyme responsible for bilirubin generation, appears to decrease in insulin-resistant conditions (Abraham et al. 2008; Belo et al. 2014). Kim et al. (2014) focused on Korean adults, women and men. Of the Korean adults with normal weight, approximately 20% were identified as having normal weight obesity based on body composition analysis using methods such as dual-energy X-ray absorptiometry (DEXA) or BIA. In addition, it was found that individuals with NWO were more likely to have cardiometabolic risk factors than normal weight lean individuals without excess adiposity, including elevated blood pressure, dyslipidemia, insulin resistance and inflammatory markers. In addition, another study by Bellissimo et al. (2019) showed that individuals with NWO had different patterns of metabolites compared to lean individuals. Metabolites associated with lipid metabolism, such as free fatty acids and phospholipids, were elevated in the plasma of individuals with NWO, indicating altered lipid homeostasis and possible dysregulation of lipid metabolic pathways. In addition, metabolites involved in glucose metabolism, such as amino acids and glycolytic intermediates, showed a different abundance in the two groups, suggesting possible differences in energy metabolism and insulin sensitivity. These findings highlight the utility of high-resolution plasma metabolomics in elucidating metabolic disturbances associated with NWO and provide insights into the underlying metabolic pathways contributing to this condition. Although the study by Berg et al. (2015) was conducted in a Swedish population of women and men, we can observe that a wide range of body fat was present in normal weight individuals. Women with NWO had higher serum triglyceride levels, low density cholesterol, C-reactive protein, apolipoprotein B and apolipoprotein B/A-I ratio compared to the normal weight group.

This study has several limitations that should be acknowledged. First, due to the cross-sectional design, it is not possible to establish causal relationships between NWO and differences in lipid profile. Longitudinal studies would be necessary to determine causality. Second, the study population was limited to middle-aged Slovakian women, which may limit the generalizability of the findings to other populations and age groups. Third, the binary categorization of physical activity has its limitations as it does not take into account the duration, intensity, and frequency of physical activity, which are crucial factors in evaluating its influence on body composition and metabolic health. Finally, the use of volunteer-based recruitment can introduce biases and may not ensure population representativeness. Despite these limitations, this study provides valuable insights into the metabolic disturbances associated with NWO and underscores the importance of recognizing this phenotype in clinical practice to prevent related health issues. Further research is needed to explore the underlying mechanisms and to develop effective interventions for individuals with NWO.

Conclusion

In conclusion, this study reveals significant differences in body composition and fat distribution between NWL and NWO groups and highlights the importance of waist circumference as a measure of central adiposity. In addition, significant differences were found in serum uric acid levels between the aforementioned groups, with significantly higher levels observed in the NWO group.

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Conflict of interests

The authors declare that there is no conflict of interest.

Ethical approval

Each participant provided written informed consent for this study which adhered to the Declaration of Helsinki principles.

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Authors' contribution

DF and SS contributed to the study conception, design, performance, and the manuscript's writing. PŠ and AH participated in data collection and manuscript writing. All authors saw and approved the final version of the manuscript.

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