Hormonal, Body Composition, and Biochemical Correlates of Menopausal Symptoms in Obese Postmenopausal Women

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Abstract. Background: Menopausal symptom severity is influenced by hormonal, metabolic, and inflammatory factors; however, their relative contributions remain incompletely understood. This exploratory study investigated the associations of body composition, serum estradiol, total cholesterol, and tumor necrosis factor-alpha (TNF-α) with menopausal symptom severity in obese postmenopausal women. Methods: This exploratory cross-sectional study involved 30 postmenopausal women with obesity aged 50–55 years. Menopausal symptom severity was evaluated with the Menopause Rating Scale (MRS), with body composition and biochemical parameters assessed according to standard procedures. Potential factors related to menopausal symptom severity were explored using correlation and multiple linear regression. Results: Among the variables examined, serum estradiol showed a significant inverse association with total MRS score and remained independently associated with menopausal symptom severity after adjustment for body fat percentage, total cholesterol, and TNF-α ($\beta = -0.688$, $p < 0.001$). The regression model explained 68.0% of the variance in MRS score (adjusted $R^2 = 0.628$). Total cholesterol was associated with MRS only in the unadjusted analysis, whereas body composition parameters and TNF-α were not independently associated with menopausal symptom severity. Conclusions: These exploratory findings suggest that serum estradiol may be more closely associated with menopausal symptom severity than body composition, lipid profile, or TNF-α in obese postmenopausal women.

Keywords: Body Composition, Estradiol, Menopause Rating Scale, Obesity, Tumor Necrosis Factor-alpha.

1 Introduction

Menopause is clinically defined as the absence of menstruation for at least 12 months following the loss of ovarian follicular function [1,2]. This transition is accompanied

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K. M. Ariesaka and D. Fauziah (eds.), *Proceedings of the 3rd Malang International Conference on Medical and Health Sciences (MICROMEDHS 2026)*, Advances in Health Sciences Research 96,
https://doi.org/10.2991/978-94-6239-807-8_3

by profound endocrine and metabolic changes that increase cardiometabolic disorders and adversely affect overall health and well-being. Vasomotor symptoms, sleep disturbances, psychological complaints, musculoskeletal discomfort, and urogenital symptoms are commonly reported during the postmenopausal period and frequently interfere with daily functioning [3,4]. The Menopause Rating Scale (MRS), a commonly used instrument, assesses symptom severity within somatic, psychological, and urogenital domains. [5,6].

Declining estrogen production is considered the principal biological mechanism underlying menopausal symptoms because estradiol regulates thermoregulation, neurotransmission, vascular function, and maintenance of musculoskeletal and urogenital tissues [7,8]. However, symptom severity varies considerably among women with similar estradiol concentrations, suggesting that additional biological factors may contribute. Menopause is also characterized by increased adiposity, unfavorable lipid metabolism, and chronic low-grade inflammation, all of which have been proposed to influence menopausal symptoms [9,10]. Earlier research has yielded mixed findings on the independent relationships of body composition, metabolic factors, and inflammatory biomarkers with menopausal symptom severity [6,11].

Few studies have simultaneously evaluated hormonal, adiposity-related, metabolic, and inflammatory factors to determine their relative associations with menopausal symptom severity, particularly among obese postmenopausal women. This evidence gap is relevant because obesity may modify hormonal and inflammatory responses during menopause. This exploratory study aimed to investigate the associations of body composition parameters, serum estradiol, total cholesterol, and tumor necrosis factor-alpha (TNF-α) with menopausal symptom severity in obese postmenopausal women.

2 Methods

2.1 Study Design and Participants

We conducted an exploratory cross-sectional investigation involving postmenopausal women with obesity living in Surabaya, Indonesia. Participants were 50–55 years old, had experienced natural menopause for 12–36 months, had a BMI ≥25 kg/m² according to the Asia-Pacific classification, serum estradiol concentrations below 30 pg/mL, and reported a sedentary lifestyle. Women were not included if they had recently received hormone replacement therapy, used medications that could influence menopausal symptoms, had relevant cardiovascular, endocrine, hepatic, renal, inflammatory, or musculoskeletal disorders, smoked, consumed alcohol, or had incomplete study data.

The Faculty of Medicine at Universitas Airlangga in Surabaya, Indonesia's Health Research Ethics Committee approved this study (Approval No. 06/EC/KEPK/FKUA/2025). All participants provided written informed consent, and the study procedures adhered to the principles of the Declaration of Helsinki.

2.2 Measurement

Body weight, height, BMI, waist circumference, body fat percentage (BFP), and fat mass (FM) were among the anthropometric measurements. Assessment of body composition was performed by bioelectrical impedance analysis following the manufacturer's recommended procedures. Samples of venous blood were obtained for biochemical examinations. Electrochemiluminescence immunoassay (ECLIA) was used to measure serum estradiol concentrations; point-of-care testing (POCT) was used to measure total cholesterol using the AutoCheck 3-in-1 Multi-Monitoring System (Onemed, Indonesia); and a high-sensitivity ELISA kit (Cat. No. E0082Hu; BT Laboratory, Shanghai, China) was used to measure TNF-α.

Menopausal symptoms were assessed with the validated Indonesian version of the MRS, an 11-item instrument covering somatic, psychological, and urogenital domains. More severe menopausal symptoms are indicated by higher overall scores.

2.3 Statistical Analysis

Data analysis were conducted in SPSS version 30.0 (IBM Corp., Armonk, NY, USA). Numerical variables were described using either mean ± standard deviation or median (IQR), as appropriate to their distributions. Relationships between MRS scores and participant characteristics were assessed using Pearson or Spearman correlation coefficients according to data distribution. Candidate predictors identified from the bivariate analysis and biological considerations were subsequently evaluated in a multivariable linear regression model. Model assumptions were examined before interpretation. A p-value below 0.05 was considered statistically significant.

3 Results

The analysis included 30 postmenopausal women with obesity. Table 1 summarizes their demographic, body composition, biochemical, and menopausal symptom characteristics at baseline.

Table 1. Demographic, Body Composition, Biochemical, and Menopausal Symptom Characteristics of the Participants.

Variable	Median (IQR)	Min–Max
Demographic characteristic		
Age, years	53 (51–53)	50–55
Body-composition parameters		
Body mass index, kg/m²	28.85 (26.35–30.08)	25.20–36.71
Waist circumference, cm	93 (90–104)	85–106
Body fat percentage, %	42.40 (38.80–43.50)	34.00–57.90
Fat mass, kg	28.21 (24.55–32.93)	18.77–53.07
Biochemical parameters		
Estradiol, pg/mL	10.70 (8.31–14.40)	5.67–19.40
Total cholesterol, mg/dL	193 (184–200)	143–248

Variable	Median (IQR)	Min–Max
TNF-α, Ng/L	129.22 (104.84–168.10)	52.59–348.10
Menopausal symptoms		
Total MRS score	13 (10–17)	5–28

Note: BMI, body mass index; TNF-α, tumor necrosis factor-alpha; MRS, Menopause Rating Scale; IQR, interquartile range

The relationships between participant characteristics and menopausal symptom severity are presented in Table 2. Among the variables evaluated, estradiol concentration demonstrated a significant inverse association with total MRS score, whereas total cholesterol showed a significant positive association. No significant relationships were observed between menopausal symptom severity and age, body mass index, waist circumference, BFP, fat mass, or TNF-α concentration.

Table 2. Associations between participant characteristics and total MRS score.

Variable	Correlation coefficient	p-value
Age	ρ = 0.227	0.227
Body mass index	ρ = 0.026	0.893
Waist circumference	ρ = 0.066	0.730
Body fat percentage	ρ = 0.120	0.528
Fat mass	ρ = 0.003	0.986
Estradiol	r = −0.787	<0.001*
Total cholesterol	ρ = 0.414	0.023*
TNF-α	ρ = 0.153	0.420

Note: Pearson's correlation was applied to estradiol because both estradiol and total MRS score were normally distributed; Spearman's rank correlation was used for all other variables. * Indicates statistical significance ($p < 0.05$).

To further characterize the association between estradiol and menopausal symptoms, correlations were examined across individual MRS domains (Table 3). Lower estradiol concentrations were consistently associated with greater symptom severity across all menopausal domains. The strongest association was observed for psychological symptoms, followed by urogenital and somatic symptoms.

Table 3. Associations between estradiol concentration and MRS domains.

MRS domain	Spearman's ρ	p-value
Somatic domain	−0.457	0.011*
Psychological domain	−0.657	<0.001*
Urogenital domain	−0.513	0.004*

Note: MRS, Menopause Rating Scale. * Indicates statistical significance ($p < 0.05$).

Multiple linear regression was used to assess the independent associations of serum estradiol, total cholesterol, TNF-α, and BFP with total MRS score. Variables were selected based on biological relevance and bivariate findings (Table 4). After adjustment, estradiol remained the only independently associated factor, with no evidence of multicollinearity.

Table 4. Multiple linear regression analysis of factors associated with total MRS score.

Predictor	B	SE	Standardized β	95% CI for B	p-value	VIF
Estradiol, pg/mL	−0.990	0.184	−0.688	−1.368 to −0.612	**<0.001**	1.270
Total cholesterol, mg/dL	0.067	0.039	0.223	−0.013 to 0.147	0.097	1.305
TNF-α, Ng/L	0.006	0.009	0.075	−0.012 to 0.024	0.528	1.083
Body fat percentage, %	0.121	0.116	0.121	−0.118 to 0.360	0.306	1.042

Model statistics: R = 0.824; R^2 = 0.680; adjusted R^2 = 0.628; standard error of the estimate = 3.522; F(4,25) = 13.262; p < 0.001. B, unstandardized regression coefficient; SE, standard error; β, standardized regression coefficient; CI, confidence interval; VIF, variance inflation factor; MRS, Menopause Rating Scale; TNF-α, tumor necrosis factor alpha

4 Discussion

The current study demonstrated that serum estradiol was the only independent factor associated with menopausal symptom severity after adjustment for BFP, total cholesterol, and TNF-α. In contrast, body composition parameters, inflammatory status, and lipid profile were not independently associated with menopausal symptoms. These results indicate that hormonal factors may be more closely related to menopausal symptom severity than metabolic or inflammatory factors in postmenopausal women with obesity.

The inverse association between estradiol concentration and severity of mmenopausal symptom observed in this study is biologically plausible and consistent with current understanding of menopausal physiology. Estrogen regulates hypothalamic thermoregulation, serotonergic and noradrenergic neurotransmission, endothelial function, bone remodeling, and maintenance of urogenital tissues. Consequently, declining estradiol concentrations contribute to vasomotor symptoms, psychological disturbances, sleep impairment, musculoskeletal discomfort, and urogenital atrophy[12–14].

The present results support previous observations linking lower circulating estradiol concentrations with a greater burden of menopausal symptoms, including findings reported by Kaur et al. (2017)[7]. Likewise, Downes et al. (2025) emphasized that estrogen deficiency remains the principal biological mechanism responsible for deterioration in health-related quality of life during menopause and that symptom burden is largely driven by declining estrogen levels[3]. The stronger association observed between estradiol and the psychological domain of the MRS may also reflect estrogen's role in modulating serotonin and dopamine pathways[15,16]. Estrogen influences mood regulation, cognition, sleep, and emotional processing [17].

Contrary to our initial hypothesis, after adjusting for estradiol levels and biochemical variables, body composition parameters showed no independent association with the severity of menopausal symptoms. Earlier observational research have indicated that the severity of menopausal symptoms is linked to central adiposity[6,11]. Hoang et al.

(2026) concluded that multiple demographic, lifestyle, hormonal, and metabolic factors contribute to menopausal symptoms and that the magnitude of association differs substantially across populations, symptom assessment tools, and menopausal stages[18]. These findings may partly reflect the homogeneous characteristics of our participants. All women were obese and within a narrow age range, reducing variability in anthropometric measurements. Therefore, differences in adiposity may have been insufficient to explain variations in symptom severity after hormonal status was considered.

No independent relationship was observed between TNF-α and severity of mmenopausal symptom in the present study. This finding does not necessarily contradict previous evidence but rather reflects the complexity of inflammatory mechanisms during menopause. Adipose tissue has an active endocrine role, releasing inflammatory mediators such as TNF-α that may promote persistent low-grade inflammation in postmenopausal women [19,20]. However, evidence directly linking circulating TNF-α concentrations to overall Menopause Rating Scale (MRS) severity remains limited. Thus, a single TNF-α measurement may not fully capture the complex inflammatory processes underlying menopausal symptoms.

Total cholesterol demonstrated a significant association with menopausal symptom severity in the bivariate analysis but was no longer independently associated after adjustment for estradiol, BFP, and TNF-α. The attenuation of this association suggests that the relationship between total cholesterol and menopausal symptom severity was not independent of the other biological variables included in the model. Previous studies have shown that declining estrogen concentrations after menopause are associated with adverse lipid metabolism and increased cardiovascular risk [9,21]. The loss of significance after adjustment may reflect the shared biological mechanisms linking hormonal changes, lipid metabolism, and menopausal symptoms rather than an independent effect of total cholesterol itself.

The present study simultaneously evaluated hormonal, adiposity-related, metabolic, and inflammatory factors associated with menopausal symptom severity, providing a comprehensive biological perspective in obese postmenopausal women. Among the variables examined, serum estradiol showed the strongest independent association with menopausal symptoms. However, the exploratory cross-sectional design, small sample size, and potential residual confounding limit causal inference and generalizability. Further investigation in larger prospective cohorts is warranted to confirm these results.

5 Conclusion

In this exploratory study of obese women in early postmenopause, serum estradiol was independently and inversely associated with overall and domain-specific menopausal symptom severity after adjustment for adiposity, total cholesterol, and TNF-α. No independent associations were observed for the other variables. These findings highlight the potential importance of estradiol in relation to menopausal symptoms and warrant confirmation in larger prospective studies.

Acknowledgments. The authors gratefully acknowledge the Faculty of Medicine, Universitas Negeri Malang, Indonesia, for financial support for the publication.

Disclosure of Interests. No conflicts of interest were reported by the authors..

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