THE IMPACT OF OBESITY ON THE DEVELOPMENT AND SEVERITY OF CLIMACTERIC SYNDROME IN MENOPAUSAL WOMEN: A COMPREHENSIVE LITERATURE REVIEW

G'ulomova Shahrinoz Qahramon qizi
Department of Fundamental Medicine, Asian International University
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Background and Urgency. The climacteric period is a critical physiological transition in a woman's life, characterized by the progressive cessation of ovarian function and a subsequent drastic decline in systemic estrogen levels. Globally, this demographic faces an intersecting public health crisis: the pathological rise in obesity and metabolic syndrome. In postmenopausal women, the depletion of ovarian 17β-estradiol disrupts energy homeostasis, alters lipid metabolism, and promotes a profound shift from subcutaneous to visceral adipose tissue accumulation. Consequently, obesity cannot be viewed merely as a passive comorbidity or a cosmetic issue; it functions as a highly active pathophysiological and neuroendocrine modulator that significantly exacerbates the clinical severity of climacteric syndrome (CS). Despite extensive epidemiological associations, the explicit cross-talk between adipocyte-derived signaling molecules and central neuroendocrine pathways remains a subject of intense scientific scrutiny, requiring a meticulous synthesis of contemporary literature to guide evidence-based clinical management.

Keywords: Menopause, Climacteric Syndrome, Obesity, Body Mass Index (BMI), Visceral Adiposity, Vasomotor Symptoms, Adipokines, Neuroinflammation.

Objective. The primary objective of this comprehensive literature review is to systematically evaluate, synthesize, and theoretically ground the precise pathogenetic mechanisms through which obesity modifies the development, phenotypic expression, and clinical severity of climacteric syndrome symptoms in menopausal women, thereby identifying gaps in current academic knowledge and optimizing holistic therapeutic approaches.

Pathophysiological and Endocrine Mechanisms

Historically, adipose tissue during menopause was hypothesized to exert a protective effect due to peripheral aromatization, wherein adrenal-derived androstenedione is converted into estrone by the enzyme aromatase (CYP19A1) expressed in adipocytes. While this peripheral synthesis provides a low baseline level of circulating estrogens, modern molecular endocrinology reveals that the dysregulated, hypertrophic adipocytes characteristic of obesity negate this minor compensatory advantage. Visceral obesity initiates a persistent, low-grade chronic inflammatory state within the adipose tissue, marked by the massive infiltration of macrophages and the hypersecretion of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1). These inflammatory cascades directly impair insulin receptor substrate signaling, triggering profound systemic insulin resistance and secondary compensatory hyperinsulinemia. Elevated insulin levels suppress the hepatic synthesis of sex hormone-binding globulin (SHBG), rapidly accelerating the bioavailability of free, unbound fractions of both estrogens and androgens, which further de-stabilizes the delicate homeostatic feedback loops of the hypothalamic-pituitary-ovarian axis.

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Furthermore, adipose tissue serves as a complex endocrine organ secreting specialized peptides termed adipokines, including leptin and adiponectin. In obese states, a distinct state of leptin resistance develops, resulting in markedly elevated serum leptin levels paired with a concurrent down-regulation of adiponectin, an essential insulin-sensitizing and anti-inflammatory protein. This distorted adipokine ratio directly interferes with central neuroendocrine networks. Leptin receptors are highly expressed within the arcuate nucleus and periventricular regions of the hypothalamus, where they interact closely with kisspeptin, neurokinin B, and dynorphin (KNDy) neurons. KNDy neurons serve as the primary coordinators of both gonadotropin-releasing hormone (GnRH) pulsatility and central thermoregulation. The toxic microenvironment generated by hyperleptinemia, insulin resistance, and elevated pro-inflammatory cytokines compromises KNDy neuronal integrity, thereby directly predisposing obese menopausal women to profound dysregulation of downstream autonomic and metabolic pathways.

Impact on Somato-Vegetative and Neurovegetative Symptoms

The clinical presentation of climacteric syndrome is classicized by neurovegetative symptoms, most notably vasomotor instability manifesting as hot flashes and nocturnal diaphoresis. For decades, scientific consensus debated whether obesity provided a buffer against vasomotor symptoms due to higher estrone production. However, massive international cohort studies have decisively overturned this 'estrogen cushion hypothesis,' replacing it with the modern 'thermal insulation hypothesis.' Adipose tissue possesses a remarkably low thermal conductivity, functioning as a highly effective physical insulator that impedes core body heat dissipation. In obese postmenopausal women, the core body temperature rises more rapidly, easily overshooting the significantly narrowed thermoregulatory zone maintained by the estrogen-depleted hypothalamus. To trigger heat-loss mechanisms, the autonomic nervous system initiates exaggerated peripheral vasodilation and profuse sweating, increasing both the frequency and subjective distress of hot flashes.

Beyond physical insulation, the hyperactivation of the sympathetic nervous system (SNS) in obese individuals plays an essential role. Chronic hyperleptinemia and insulin resistance act as potent stimulants of central sympathetic outflow, accelerating resting heart rates and promoting arterial blood pressure lability. This baseline autonomic hyperactivity means that any minor threshold fluctuation in the hypothalamic thermoregulatory center triggers a catastrophic, high-amplitude vasomotor event. Additionally, the clinical severity of these episodes is compounded by the structural and functional changes in the cardiovascular system frequently observed in obese women, rendering the vascular endothelium less responsive to compensatory mechanisms and intensifying the perception of cardiovascular palpitations and physical exhaustion.

Psychological and Cognitive Correlates

The intersection of obesity and climacteric syndrome extends deeply into the neuropsychiatric sphere. Menopause is widely associated with a heightened vulnerability to psychoemotional disturbances, including major depressive disorders, generalized anxiety, severe irritability, and sleep fragmentation. Literary analysis indicates that obese menopausal women exhibit a significantly elevated relative risk for severe psychological symptom scores compared to their normal-weight peers. This phenomenon is driven by a complex bi-directional pathomechanism. At the molecular level, the systemic pro-inflammatory cytokines (TNF-α and IL-6) generated by visceral adiposity are capable of crossing the blood-brain barrier, where they induce neuroinflammation, disrupt tryptophan metabolism, and reduce the synthesis of vital neurotransmitters, specifically serotonin and dopamine, within the limbic system.

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At the psychosocial level, the presence of obesity profoundly degrades health-related quality of life, exacerbates body dysmorphia, and lowers self-esteem, which collectively amplifies the baseline psychological distress of the menopausal transition. Sleep architecture is also severely disrupted; obesity is the single greatest risk factor for obstructive sleep apnea (OSA), which, when combined with severe nocturnal hot flashes, results in chronic sleep deprivation. This structural sleep fragmentation further impairs prefrontal cortex function, leading to cognitive complaints such as memory lapses, brain fog, and decreased executive function, establishing a vicious cycle where metabolic dysfunction and psychological distress continuously reinforce one another.

Conclusion and Future Perspectives

In conclusion, a meticulous synthesis of contemporary scientific literature firmly establishes that obesity is a major driving force that severely amplifies the development, clinical severity, and multi-organ manifestations of climacteric syndrome in menopausal women. The pathophysiological mechanisms are rooted in a complex synergy between estrogen deficiency and visceral adiposity, characterized by chronic neuroinflammation, altered adipokine dynamics (leptin resistance), and sympathetic nervous system hyperactivation. These factors systematically dismantle central thermoregulation and psychoemotional stability, leading to severe vasomotor, autonomic, and psychological symptoms. The theoretical frameworks highlighted in this review demonstrate that managing climacteric syndrome effectively requires shifting away from isolated hormone replacement therapies toward a comprehensive, multi-disciplinary approach. Integrating mandatory weight management, metabolic stabilization, and targeted lifestyle modifications into standard care protocols is absolutely critical to mitigating the pathological impact of obesity and safeguarding the long-term health and quality of life of menopausal women.

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