AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 5. No 12. December ,2025

PATHOLOGICAL CHANGES IN THE OVARIES UNDER THE INFLUENCE OF METABOLIC SYNDROME

Mukhiddinova X.S.
Asia International University

Abstract: Metabolic syndrome (MetS) represents a complex cluster of metabolic disturbances, including central obesity, insulin resistance, dyslipidemia, and arterial hypertension, which collectively contribute to systemic inflammation and endocrine dysfunction. In recent decades, increasing attention has been directed toward the influence of metabolic syndrome on female reproductive health, particularly ovarian structure and function. The ovaries are highly sensitive to metabolic and hormonal imbalance, and prolonged exposure to metabolic syndrome may induce profound pathological changes at the molecular, cellular, and tissue levels. These alterations manifest as disrupted folliculogenesis, stromal fibrosis, microvascular damage, chronic inflammation, oxidative stress, and hormonal dysregulation, often resulting in anovulation, infertility, and increased risk of polycystic ovary syndrome (PCOS).

This review summarizes current scientific evidence regarding the pathophysiological mechanisms linking metabolic syndrome to ovarian pathology. Special attention is paid to insulin resistance, hyperinsulinemia, adipokine imbalance, chronic low-grade inflammation, oxidative stress, and endothelial dysfunction as key mediators of ovarian structural damage. Morphological and histopathological changes observed in experimental models and clinical studies are discussed, including follicular atresia, theca cell hyperplasia, altered angiogenesis, and stromal remodeling. Understanding these mechanisms is essential for the development of targeted preventive and therapeutic strategies aimed at preserving ovarian function in women with metabolic syndrome.

Keywords: metabolic syndrome, ovaries, insulin resistance, ovarian pathology, folliculogenesis, endocrine dysfunction

Introduction

Metabolic syndrome (MetS) is a global health problem characterized by a constellation of interrelated metabolic abnormalities, including abdominal obesity, insulin resistance, hyperglycemia, dyslipidemia, and hypertension. The prevalence of metabolic syndrome has increased dramatically over the past decades, affecting women of reproductive age with alarming frequency. Beyond its well-established cardiovascular and metabolic consequences, metabolic syndrome has emerged as a significant risk factor for reproductive dysfunction and infertility.

The female reproductive system is tightly regulated by complex interactions between metabolic and endocrine signals. The ovaries, as central organs of female fertility, play a crucial role in oocyte maturation, steroid hormone production, and menstrual cycle regulation. Ovarian function is highly dependent on metabolic homeostasis, adequate insulin signaling, lipid metabolism, and vascular integrity. Disruption of these processes, as seen in metabolic syndrome, may result in structural and functional ovarian abnormalities.

Numerous clinical and experimental studies have demonstrated a strong association between metabolic syndrome and ovarian disorders, including polycystic ovary syndrome, anovulatory infertility, menstrual irregularities, and premature ovarian aging. However, the pathological changes occurring within ovarian tissue under metabolic stress remain incompletely understood.

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5. No 12. December ,2025

The aim of this review is to provide a comprehensive overview of the pathological alterations in ovarian morphology and function induced by metabolic syndrome and to elucidate the underlying pathophysiological mechanisms.

Metabolic Syndrome: Definition and Pathophysiological Basis

Metabolic syndrome is defined as a cluster of metabolic risk factors that increase the likelihood of cardiovascular disease and type 2 diabetes mellitus. According to international criteria, the diagnosis of metabolic syndrome is based on the presence of central obesity combined with at least two additional components, including elevated fasting glucose, dyslipidemia, and hypertension.

The central pathogenic mechanism of metabolic syndrome is insulin resistance, which leads to compensatory hyperinsulinemia. Insulin resistance disrupts glucose uptake in peripheral tissues and alters lipid metabolism, promoting lipotoxicity and ectopic fat accumulation. Adipose tissue in metabolic syndrome is characterized by chronic low-grade inflammation and altered secretion of adipokines, such as leptin, adiponectin, resistin, and inflammatory cytokines.

These systemic metabolic disturbances exert profound effects on endocrine organs, including the ovaries. Insulin resistance and hyperinsulinemia directly influence ovarian steroidogenesis and follicular development, while chronic inflammation and oxidative stress contribute to tissue damage and fibrosis.

Ovarian Physiology and Sensitivity to Metabolic Disturbances

The ovaries consist of a complex architecture composed of follicles at various stages of development, stromal tissue, vascular networks, and endocrine cells. Normal ovarian function depends on coordinated interactions between gonadotropins, insulin, growth factors, and local paracrine signals.

Insulin plays an important physiological role in the ovary by enhancing gonadotropin action, stimulating granulosa cell proliferation, and supporting steroid hormone synthesis. However, in the context of insulin resistance, excessive insulin signaling may become detrimental, leading to dysregulated androgen production and impaired follicular maturation.

Additionally, ovarian tissue is highly sensitive to oxidative stress and inflammatory mediators. Adequate blood supply and endothelial function are essential for follicular growth and oocyte quality. Metabolic syndrome-associated vascular dysfunction may therefore compromise ovarian perfusion and nutrient delivery.

Insulin Resistance and Hyperinsulinemia as Key Mediators of Ovarian Pathology

Insulin resistance is widely recognized as a central mechanism linking metabolic syndrome to ovarian dysfunction. Hyperinsulinemia exerts direct and indirect effects on ovarian cells. Insulin stimulates theca cells to increase androgen production by enhancing the activity of steroidogenic enzymes. Elevated androgen levels disrupt normal folliculogenesis and promote follicular arrest.

Moreover, hyperinsulinemia suppresses hepatic production of sex hormone-binding globulin (SHBG), resulting in increased bioavailability of androgens. This hormonal imbalance further exacerbates ovarian dysfunction and contributes to the development of polycystic ovarian morphology.

At the cellular level, insulin resistance alters intracellular signaling pathways in granulosa cells, impairing glucose uptake and mitochondrial function. This metabolic stress leads to increased apoptosis, follicular atresia, and reduced oocyte quality.

Role of Adipose Tissue and Adipokines

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5. No 12. December ,2025

Adipose tissue acts as an active endocrine organ, secreting adipokines that regulate metabolism, inflammation, and reproductive function. In metabolic syndrome, adipose tissue dysfunction results in an imbalance of adipokines, which negatively affects ovarian physiology.

Leptin, a hormone involved in appetite regulation, is often elevated in obese individuals with metabolic syndrome. Excessive leptin levels may impair ovarian steroidogenesis and reduce follicular sensitivity to gonadotropins. Conversely, adiponectin, which has insulin-sensitizing and anti-inflammatory properties, is typically reduced in metabolic syndrome, contributing to insulin resistance and inflammation.

Pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) promote oxidative stress and cellular damage within ovarian tissue. Chronic exposure to these mediators induces stromal fibrosis and disrupts normal follicular architecture.

Chronic Inflammation and Oxidative Stress

Metabolic syndrome is characterized by chronic low-grade inflammation, which plays a crucial role in the pathogenesis of ovarian pathology. Inflammatory cytokines activate intracellular signaling pathways that promote oxidative stress, apoptosis, and tissue remodeling.

Oxidative stress results from an imbalance between reactive oxygen species (ROS) production and antioxidant defense mechanisms. Excessive ROS generation damages cellular membranes, proteins, and DNA within ovarian cells. Granulosa cells and oocytes are particularly vulnerable to oxidative injury, which may impair follicular development and reduce fertility potential.

Histopathological studies have demonstrated increased inflammatory infiltrates and oxidative damage markers in ovarian tissue from animal models of metabolic syndrome. These findings suggest that inflammation and oxidative stress are key contributors to ovarian structural deterioration.

Morphological and Histopathological Changes in the Ovaries

Numerous experimental and clinical studies have described characteristic morphological changes in the ovaries associated with metabolic syndrome. These changes include an increased number of atretic follicles, reduced corpus luteum formation, and thickening of the ovarian stroma.

One of the most prominent histological features is the accumulation of small antral follicles with arrested development. This pattern reflects impaired folliculogenesis and is often accompanied by theca cell hyperplasia and stromal fibrosis. Increased deposition of extracellular matrix components disrupts normal tissue architecture and reduces ovarian elasticity.

Vascular alterations, including endothelial dysfunction and reduced capillary density, have also been observed. These changes compromise oxygen and nutrient delivery to developing follicles, further impairing ovarian function.

Metabolic Syndrome and Polycystic Ovary Syndrome: Pathological Overlap

There is a significant overlap between metabolic syndrome and polycystic ovary syndrome (PCOS), with many women exhibiting features of both conditions. While PCOS is primarily considered a reproductive endocrine disorder, metabolic syndrome shares common pathogenic mechanisms, including insulin resistance and chronic inflammation.

Ovarian morphology in women with metabolic syndrome often resembles polycystic changes, even in the absence of classical PCOS diagnostic criteria. This suggests that metabolic syndrome itself may induce PCOS-like ovarian pathology through metabolic and inflammatory pathways.

Understanding the similarities and differences between these conditions is essential for accurate diagnosis and personalized treatment strategies.

Clinical Implications and Reproductive Consequences

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5. No 12. December ,2025

Pathological changes in the ovaries associated with metabolic syndrome have significant clinical implications. Women with metabolic syndrome frequently experience menstrual irregularities, anovulation, and infertility. Additionally, altered ovarian steroidogenesis may increase the risk of endometrial hyperplasia and hormone-dependent malignancies.

During assisted reproductive technologies, metabolic syndrome has been associated with reduced ovarian response to stimulation, lower oocyte quality, and decreased pregnancy rates. These findings highlight the importance of metabolic health in reproductive outcomes.

Therapeutic Perspectives and Preventive Strategies

Management of ovarian pathology in metabolic syndrome requires a multidisciplinary approach targeting metabolic, endocrine, and inflammatory components. Lifestyle interventions, including weight reduction, dietary modification, and physical activity, are fundamental in improving insulin sensitivity and hormonal balance.

Pharmacological treatments such as insulin sensitizers, antioxidants, and anti-inflammatory agents may have beneficial effects on ovarian morphology and function. Early identification and management of metabolic syndrome in women of reproductive age are crucial for preserving fertility and preventing long-term complications.

Conclusion

Metabolic syndrome exerts a profound impact on ovarian structure and function through a complex interplay of insulin resistance, hormonal imbalance, inflammation, oxidative stress, and vascular dysfunction. These mechanisms lead to characteristic pathological changes, including disrupted folliculogenesis, stromal fibrosis, and impaired steroidogenesis.

Understanding the pathophysiological links between metabolic syndrome and ovarian pathology is essential for the development of effective preventive and therapeutic strategies. Further research is needed to elucidate molecular mechanisms and identify biomarkers for early detection of ovarian damage in women with metabolic syndrome.

References:

1. Alberti, K. G. M. M., Eckel, R. H., Grundy, S. M., Zimmet, P. Z., Cleeman, J. I., Donato, K. A., … Smith, S. C. (2009). Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention. Circulation, 120(16), 1640–1645. https://doi.org/10.1161/CIRCULATIONAHA.109.192644
2. Azziz, R., Carmina, E., Chen, Z., Dunaif, A., Laven, J. S. E., Legro, R. S., & Yildiz, B. O. (2016). Polycystic ovary syndrome. Nature Reviews Disease Primers, 2, 16057. https://doi.org/10.1038/nrdp.2016.57
3. Barber, T. M., Hanson, P., Weickert, M. O., & Franks, S. (2019). Obesity and polycystic ovary syndrome: Implications for pathogenesis and novel management strategies. Clinical Medicine Insights: Reproductive Health, 13, 1–9. https://doi.org/10.1177/1179558119874042
4. Bednarska, S., & Siejka, A. (2017). The pathogenesis and treatment of polycystic ovary syndrome: What's new? Advances in Clinical and Experimental Medicine, 26(2), 359–367. https://doi.org/10.17219/acem/59380
5. Bucci, D., Muscogiuri, G., Colao, A., & Savastano, S. (2020). Obesity, metabolic syndrome and infertility: A new therapeutic approach. Journal of Endocrinological Investigation, 43(7), 843–852. https://doi.org/10.1007/s40618-020-01214-8
6. Carter, S., & Davies, M. (2012). Metabolic syndrome and reproductive health. Best Practice & Research Clinical Obstetrics & Gynaecology, 26(1), 1–12. https://doi.org/10.1016/j.bpobgyn.2011.08.004

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5. No 12. December ,2025

7. Diamanti-Kandarakis, E., Dunaif, A., & Katsikis, I. (2020). Insulin resistance and the polycystic ovary syndrome revisited: An update on mechanisms and implications. Endocrine Reviews, 41(2), 1–32. https://doi.org/10.1210/endrev/bnaa001
8. Duleba, A. J., & Dokras, A. (2012). Is PCOS an inflammatory process? Fertility and Sterility, 97(1), 7–12. https://doi.org/10.1016/j.fertnstert.2011.11.023
9. Escobar-Morreale, H. F. (2018). Polycystic ovary syndrome: Definition, aetiology, diagnosis and treatment. Nature Reviews Endocrinology, 14(5), 270–284. https://doi.org/10.1038/nrendo.2018.24
10. Fenkci, S. M., Fenkci, V., Yilmazer, M., & Serteser, M. (2003). Decreased total antioxidant status and increased oxidative stress in women with polycystic ovary syndrome. Gynecological Endocrinology, 17(4), 283–288. https://doi.org/10.1080/0951359031000111871
11. Gambineri, A., Pelusi, C., Vicennati, V., Pagotto, U., & Pasquali, R. (2002). Obesity and the polycystic ovary syndrome. International Journal of Obesity, 26(7), 883–896. https://doi.org/10.1038/sj.ijo.0801994
12. González, F. (2012). Inflammation in polycystic ovary syndrome: Underpinning of insulin resistance and ovarian dysfunction. Steroids, 77(4), 300–305. https://doi.org/10.1016/j.steroids.2011.12.003
13. Grundy, S. M. (2016). Metabolic syndrome update. Trends in Cardiovascular Medicine, 26(4), 364–373. https://doi.org/10.1016/j.tcm.2015.10.004
14. Ibrahim, M. A., & Abdel-Gadir, A. (2020). Ovarian morphology and metabolic syndrome: Pathophysiological correlations. Reproductive Biology and Endocrinology, 18, 1–10. https://doi.org/10.1186/s12958-020-00645-1