DOI 10.66073/ReFocus-Conf/3010123

OVARIAN FIBROSIS IN POLYCYSTIC OVARY SYNDROME: TRANSLATIONAL PERSPECTIVES ON MOLECULAR BIOMARKERS AND CHALLENGES IN NON-INVASIVE DIAGNOSIS

Sameer Aymen
Tashkent State Medical University, Undergraduate Student, Tashkent, Uzbekistan, E-mail: aymen.s2722@gmail.com

Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine and metabolic disorder characterized by hyperandrogenism, insulin resistance, chronic inflammation, and oxidative stress. The convergence of these factors activates profibrotic pathways, including transforming growth factor-beta (TGF-β)/Smad, Wnt/β-catenin, and PI3K/Akt signaling pathways, resulting in fibroblast activation, extracellular matrix (ECM) remodeling, collagen deposition, and ovarian stiffening [1]. Experimental studies have consistently demonstrated ovarian fibrosis mediated by these profibrotic pathways, including increased expression of TGF-β and connective tissue growth factor (CTGF), collagen deposition, and myofibroblast activation, ultimately contributing to progressive ovarian fibrosis and stiffening [1,2]. While human studies have primarily investigated non-invasive imaging and circulating biomarkers, evidence from histological evaluation remains limited and is largely restricted to surgically obtained ovarian specimens. Consequently, the assessment of ovarian fibrosis remains challenging because of the lack of standardized diagnostic criteria and the limited accessibility of ovarian tissue [3]. This highlights the need to understand the translational barriers that currently prevent the development of a clinically validated, non-invasive, fibrosis-specific diagnostic standard despite promising molecular biomarkers and elastographic techniques. This review aims to summarize the current evidence on non-invasive approaches to assessing ovarian fibrosis in women with PCOS and to highlight the major translational gaps between animal evidence and human clinical application.

Keywords: PCOS, ovarian fibrosis, extracellular matrix, shear wave elastography, and biomarkers.

Methods

A narrative review of human and animal studies published between 2020 and 2026 was conducted. Relevant literature was identified using databases including PubMed, Google Scholar, and other peer-reviewed sources.

Results and discussion

Animal studies: In DHEA-induced PCOS rat models, ovarian fibrosis was found to be mediated by the TGF-β signaling pathway. Fibrotic markers, including TGF-β, CTGF, fibronectin (FN), collagen, and α-SMA, were investigated following treatment with the TGF-β receptor I inhibitor SB431542 and were found to be upregulated [4]. An imbalance between matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs), whose intricate interplay plays an important role in ECM turnover, further contributed to abnormal ECM remodeling. Similar findings were reported in another experimental study in which molecular analyses of rats with PCOS demonstrated increased CTGF expression and elevated protein levels. In addition, the study reported

FOR CITATION
Sameer A. Ovarian fibrosis in polycystic ovary syndrome: translational perspectives on molecular biomarkers and challenges in non-invasive diagnosis // Proceedings of the Republican Scientific and Practical Conference “Status and Development Prospects of Fundamental and Applied Microbiology: The Viewpoint of Young Scientists”. – Tashkent, 2026. – P. 437–438.
DOI: https://doi.org/10.66073/ReFocus-Conf/3010123

increased ovarian stiffness in PCOS rats using transabdominal two-dimensional ultrasound and shear wave elastography (SWE), which corresponded with extensive collagen deposition demonstrated by Masson's trichrome staining [2]. These findings suggest that ovarian fibrosis contributes to increased ovarian stiffness. Therefore, animal models provide strong evidence for the existence of ovarian fibrosis in PCOS through combined histological and molecular evidence.

Human studies: In women diagnosed with PCOS, increased ovarian stiffness has been detected using transvaginal ultrasound and SWE [2]. Although SWE demonstrates potential diagnostic utility in PCOS, its role as a surrogate marker for ovarian fibrosis remains unvalidated because ovarian stiffness has not yet been correlated with ovarian fibrosis using an accepted histological reference standard in humans. Furthermore, stiffness measurements can be influenced by several factors, including patient heterogeneity, the stage of PCOS progression, and differences in hormonal therapy. Circulating biomarkers are also promising because they offer a non-invasive approach; however, they lack ovarian specificity and may be influenced by systemic conditions. Consequently, the absence of validated diagnostic cut-off values, lack of standardization, and limited longitudinal evidence mean that these methods should currently be regarded as potential indicators rather than validated fibrosis-specific diagnostic tools for ovarian fibrosis in women with PCOS.

Conclusion

These limitations highlight the need for further research to establish appropriate diagnostic cut-off values. Future studies should include larger sample sizes and multicenter data collection to reduce bias and improve the reliability of findings. Particular emphasis should be placed on developing standardized diagnostic criteria and validating their accuracy against an accepted reference standard. Longitudinal studies are needed to determine whether these markers accurately reflect the progression of ovarian fibrosis. Studies should also evaluate the generalizability of these approaches for diagnosing ovarian fibrosis and their feasibility for routine clinical practice. Addressing these gaps could facilitate the development of clinically applicable, non-invasive approaches for assessing ovarian fibrosis and provide a foundation for more precise and targeted therapeutic approaches.

References

1. Edepli BG, Yaba A. Molecular mechanisms of ovarian fibrosis. Mol Hum Reprod. 2026;32(1):gaaf058. doi:10.1093/molehr/gaaf058.
2. He Y, Deng S, Wang Y, et al. Evaluation of ovarian stiffness and its biological mechanism using shear wave elastography in polycystic ovary syndrome. Sci Rep. 2025;15:585. doi:10.1038/s41598-024-84338-8.
3. Nalkande S, Patil M, Nakhate K, Goyal S. Ovarian fibrosis in polycystic ovary syndrome: Mechanisms, evidences, and clinical implications. Differentiation. 2026;150:100976. doi:10.1016/j.diff.2026.100976.
4. Gu M, Wang Y, Yu Y. Ovarian fibrosis: molecular mechanisms and potential therapeutic targets. J Ovarian Res. 2024;17(1):139. doi:10.1186/s13048-024-01448-7.