

## Could the estrobolome have a role in endometriosis pathogenesis and infertility? A systematic review.

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### ABSTRACT

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**BACKGROUND:** Endometriosis is a chronic, estrogen-dependent condition affecting 10% of reproductive-aged women, often associated with infertility and chronic pelvic pain. Recent evidence suggests that gut microbiota dysbiosis and alterations in the estrobolome, defined as the collection of bacterial genes involved in estrogen metabolism, may play a role in the pathogenesis of endometriosis and infertility.

**METHODS:** This systematic review was registered with PROSPERO (ID: CRD42024627464). A comprehensive search was conducted across PubMed, Embase, Scopus, Web of Science, Cochrane CENTRAL, ClinicalTrials.gov, and grey literature sources up to December 2024, without a lower date limit. The search included terms such as "estrobolome," "endometriosis," "infertility," and "estrogen metabolism". Original articles and clinical trials investigating the role of the estrobolome in endometriosis pathogenesis and infertility were included. Abstract-only studies, reviews, and non-English articles were excluded.

**RESULTS:** Five studies were analyzed, highlighting gut dysbiosis, estrobolome alterations, and immunological factors in endometriosis and infertile patients. Some investigations reported dysregulated or increased  $\beta$ -glucuronidase activity, suggesting a potential link between microbial estrogen metabolism and disease pathophysiology. These microbial and enzymatic alterations were accompanied by elevated inflammatory cytokines and persistent activation of immune cells, possibly contributing to local and systemic estrogen stimulation and lesion progression.

**CONCLUSIONS:** Our analysis emphasizes how disruptions in estrogen-metabolizing bacterial pathways may contribute to the inflammatory and hormonal features observed in endometriosis and infertility. Given the associations observed, future studies should explore whether modulating the microbiota or estrogen metabolism can improve clinical outcomes in patients with endometriosis or infertility.