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INPLASY

miRNA in endometriosis- a new hope or illusion

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 June 2025 and was last updated on 7 June 2025.

INTRODUCTION

Review question / Objective Population (P): Women with surgically and histopathologically confirmed endometriosis
Intervention (I): Detection of specific circulating and tissue-based microRNAs (miRNAs)
Comparator (C): Women without endometriosis (e.g., asymptomatic or undergoing surgery for other benign gynecologic conditions)
Outcome (O): Diagnostic accuracy and expression differences of miRNAs
Study design (S): Clinical studies (prospective, retrospective), randomized trials, meta-analyses

Objective:
To evaluate the diagnostic potential of circulating and tissue-specific microRNAs as non-invasive biomarkers for endometriosis by systematically reviewing and analyzing the current literature.

Rationale Endometriosis is a prevalent and often debilitating gynecological disorder lacking reliable, non-invasive diagnostic methods. Although imaging techniques have improved, laparoscopy remains the diagnostic gold standard—an invasive and costly procedure. Therefore, identifying accurate, reproducible, and non-invasive biomarkers is a clinical priority.
MicroRNAs (miRNAs), due to their regulatory functions in inflammation, cell growth, and hormonal pathways, and their stability in biological fluids, have emerged as promising candidates. Several studies have suggested miRNAs as diagnostic tools; however, methodological heterogeneity and lack of reproducibility limit their clinical application.
This review aims to critically appraise and synthesize available evidence regarding dysregulated miRNAs in endometriosis to determine whether these molecules can truly serve as reliable, non-invasive diagnostic biomarkers.

Condition being studied Endometriosis is a chronic, estrogen-dependent inflammatory condition characterized by the growth of endometrial-like tissue outside the uterus, leading

to pain, infertility, and reduced quality of life. It affects up to 10% of reproductive-age women and often causes delayed diagnosis due to nonspecific symptoms. Despite its burden, diagnostic confirmation still relies largely on invasive surgical methods, underscoring the urgent need for non-invasive diagnostic alternatives.

METHODS

Search strategy Electronic databases: PubMed and Google Scholar
Search period: 2010 to March 2025
Language: English
Keywords: “microRNA”, “miRNA”, “biomarker”, “endometriosis”, “mcRNA”, and their combinations using Boolean operators (AND/OR)
Manual search: Bibliographies of included studies
Number of initially identified studies: 727
Final included studies: 17 (after screening, duplication removal, and applying inclusion/exclusion criteria).

Participant or population Women of reproductive age with surgically and histopathologically confirmed endometriosis. Control participants included women without endometriosis, often undergoing surgery for other gynecological conditions or healthy asymptomatic women in limited cases.

Intervention Evaluation of microRNA (miRNA) expression levels in various biological samples (serum, plasma, endometrial tissue) to assess their diagnostic value in detecting endometriosis.

Comparator Control groups included women without endometriosis—either undergoing laparoscopy for other gynecologic conditions or, in one study, healthy non-operated women.

Study designs to be included Randomized clinical trials, meta-analyses, prospective and retrospective clinical studies.

Eligibility criteria Inclusion: Human studies in English (2010–2025), full-text access, sample size ≥ 24, studies with blood or endometrial tissue samples, journal Impact Factor ≥ 2
Exclusion: Non-human studies, reviews, languages other than English, inaccessible full-texts, sample size < 24, Impact Factor < 2.

Information sources PubMed, Google Scholar. Manual reference list searches from included articles. No trial registries or grey literature were included.

Main outcome(s) The primary outcome was the identification of specific circulating or tissue-based miRNAs consistently dysregulated in women with endometriosis, and their potential as diagnostic biomarkers. The review evaluated expression patterns, sensitivity/specificity (if reported), and reproducibility across studies.

Additional outcome(s) Secondary outcomes included the impact of sample type (serum, plasma, tissue), menstrual cycle phase, validation methods, and geographical distribution of studies on the reliability of miRNA detection.

Data management Two independent reviewers conducted screening and data extraction using a predefined Microsoft Excel form. Any disagreements were resolved through discussion. Data collected included study details, participant demographics, sample types, miRNA expression, menstrual cycle consideration, and main outcomes.

Quality assessment / Risk of bias analysis The risk of bias was assessed qualitatively through evaluation of study design, sample size, selection of control groups, consideration of biological variables (e.g., menstrual cycle), and transparency in validation techniques.

Strategy of data synthesis Findings were synthesized narratively due to heterogeneity in study design, miRNA types, and validation approaches. Studies were grouped and compared based on sample type, menstrual cycle consideration, and validation method (e.g., RT-qPCR, microarray). Tables were used to summarize and compare key features and findings.

Subgroup analysis Subgroup analyses were performed based on:

Sample type (serum vs. plasma vs. tissue)

Geographical origin of the study

Consideration of menstrual cycle phase

Validation method used (RT-qPCR vs. others).

Sensitivity analysis Sensitivity analysis was not performed due to the qualitative nature of the data synthesis and the heterogeneity of study methods and outcomes.

Language restriction Sensitivity analysis was not performed due to the qualitative nature of the data

synthesis and the heterogeneity of study methods and outcomes.

Country(ies) involved Department of Obstetrics & Gynecology, Institute of Medical Sciences, College of Medical Sciences, University of Rzeszow, Rzeszow, 35-959, Poland.

Keywords microRNA, miRNA, endometriosis, non-invasive biomarkers, diagnostics, gene expression, gynecology, reproductive health.

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