Endometriosis Link to Autoimmune and Inflammatory Diseases

Study Link

This was a study using data from the UK Biobank (UKBB). Researchers identified 8,223 people assigned female at birth who reported or had records of endometriosis, and compared them with a control group of UKBB participants without endometriosis, while also tracking diagnoses of immunological diseases among all participants.

Study Question

“Is there an increased risk of immunological diseases among endometriosis patients, and does a shared genetic basis contribute to this risk?”

The study evaluates 31 immunological conditions, categorized as:

• Autoimmune

• Autoinflammatory

• Mixed-pattern immune-mediated diseases

Clinical Findings

“Endometriosis patients show a significantly increased risk of autoimmune, autoinflammatory, and mixed-pattern diseases, including rheumatoid arthritis, multiple sclerosis, coeliac disease, osteoarthritis, and psoriasis.”

People with endometriosis were 30 to 80 percent more likely to have one of these immune-related diseases compared to those without endometriosis.

Genetic Findings

The study found that endometriosis shares genetic risk with several immune conditions, meaning parts of our DNA that increase endometriosis risk also increase the likelihood of these diseases.

The strongest overlaps were seen with:

• Osteoarthritis

• Rheumatoid arthritis

• Multiple sclerosis (to a lesser extent)

• Coeliac disease

• Psoriasis

A type of genetic testing called “Mendelian randomization” suggested that having endometriosis may possibly increase the risk of developing rheumatoid arthritis, indicating a potential causal link.

The researchers also identified specific shared genetic locations (loci) between endometriosis and these immune conditions, suggesting some of the same biological pathways are involved.

“Shared variants implicated biological pathways common to endometriosis and immune-mediated diseases.”

Author Conclusion

“Endometriosis patients have a moderately increased risk for osteoarthritis, rheumatoid arthritis, multiple sclerosis, coeliac disease, and psoriasis due to underlying shared biological mechanisms.”

“These findings suggest an opportunity for developing new treatments or repurposing therapies across these conditions.”

Study Limitations

“This is the first female-specific GWAS analysis for immune conditions, and statistical power is limited compared with sex-combined analyses.”

“The 39 endometriosis-associated variants used as instrumental variables explain only ~5% of the disease variation, and hence the MR causal results should be interpreted with caution.”

Overall

“These results support that endometriosis shares genetic architecture with immune-mediated diseases, such as rheumatoid arthritis and multiple sclerosis, suggesting that biological mechanisms are shared and that cross-condition therapeutic innovation may be possible.”

Another study also demonstrated a link between endo and other autoimmune conditions like hashimotos, and sjögren’s

Study #2 Link

This was a **retrospective cohort / case-control** study using two large U.S. healthcare claims databases. Authors identified **332,409** women diagnosed with Endometriosis, and compared

them with **1,220,932** matched controls without endometriosis.

- The aim was to test whether women with endometriosis had **greater odds** of being diagnosed with one of 10 different autoimmune diseases **within two years** of their endometriosis diagnosis.

Main Findings: Autoimmune Diagnoses After Endometriosis

- Among the endometriosis cohort, **4.93%** received a diagnosis of at least one autoimmune condition within two years. In contrast, only **1.42%** of the control group had an autoimmune diagnosis during the same period.

- Compared to matched controls, women with endometriosis had **roughly double the odds** of developing at least one of the 10 autoimmune diseases studied.

- The autoimmune diseases with elevated diagnosis rates included:

    - Rheumatoid arthritis

    - Hashimoto's disease

    - Systemic lupus erythematosus (SLE)

    - Multiple sclerosis (MS)

    - Pernicious anemia

    - Sjögren's syndrome

    - Myositis

    - (Also observed, though less consistently, were elevated rates for other conditions like Graves' disease and Vitiligo.)

- The increased risk was observed in both insured (commercial) and Medicaid populations, which supports generalizability across socioeconomic groups.

Interpretation by Authors

- The study provides the **first large-scale real-world evidence** that women with endometriosis have significantly elevated odds of receiving an autoimmune disease

diagnosis within a two-year window.

- This adds to a growing body of evidence that endometriosis may share biological mechanisms with autoimmune and immune-mediated diseases, including chronic inflammation, immune cell dysregulation, and systemic immune activation.

- Authors highlight that overlapping immune dysfunction (abnormal T-cell function, increased peritoneal immune cells, cytokine elevation) seen in endometriosis and autoimmune diseases supports the plausibility of this association.

Limitations & What Is Not Established

- Because of the known diagnostic delays common in both endometriosis and many autoimmune diseases, the study cannot definitively determine the **temporal order**: whether autoimmunity developed after endometriosis or whether preexisting immune dysfunction contributed. PMC+1

- The design relies on health-insurance claims data and diagnoses recorded; misdiagnosis or underdiagnosis remains possible. PMC+1

- The study does **not** prove causation — only an association. It cannot show that endometriosis causes the autoimmune diseases, or vice versa. PMC+1

What this Means for Endometriosis–Autoimmune Link

- This study strengthens the evidence that endometriosis and several autoimmune diseases co-occur at higher than expected rates.

- It suggests that clinicians and researchers should consider immune dysregulation, not just gynecologic/structural factors, when thinking about endometriosis.

- For advocacy: this supports arguments that endometriosis may belong, at least in part, to a broader class of immune-mediated disorders - and that patients with endometriosis might benefit from monitoring or therapies used for autoimmunity.

Endometriosis and the Immune System

Source: Agostinis C et al. (2021). Immunological Basis of Endometriosis. Frontiers in Immunology, 11: 599117.

Link: https://www.frontiersin.org/articles/10.3389/fimmu.2020.599117/full

DOI: 10.3389/fimmu.2020.599117

1. Endometriosis is not just hormonal; it involves the immune system.

“The risk of developing endometriosis depends on a complex interaction between genetic, immunological, hormonal, and environmental factors.”

Simplified: Hormones play a role, but the immune system and genetics are equally important. Endometriosis is now recognized as a chronic immune-inflammatory condition, not only a hormonal one.

2. How Endometriosis Forms

“Although retrograde menstruation is considered one of the main theories explaining the origin of endometriosis, this phenomenon occurs in up to 90 percent of women of reproductive age, while only 10 percent develop the disease. This discrepancy suggests that additional factors, such as defects in immune surveillance or clearance mechanisms, contribute to the establishment and persistence of endometriotic lesions.”

Simplified: Many people experience menstrual backflow, but only some develop endometriosis. This study concludes that immune dysfunction, not just tissue displacement, determines whether those cells are cleared or allowed to implant and grow.

3. Immune cells behave abnormally.

“Women with endometriosis exhibit altered functions of macrophages, lymphocytes, and natural killer cells, as well as abnormal levels of inflammatory mediators.”

Simplified: The immune cells that should recognize and remove stray endometrial-type cells do not function normally. Instead, they allow those cells to survive and promote long-term inflammation.

4. The complement system stays chronically activated.

“Alteration in the regulation of complement activation leads to chronic inflammation characteristic of endometriosis.”

Simplified: A key branch of the immune system called the complement pathway stays overactive, keeping inflammation switched on throughout the pelvis.

5. Immune overactivation occurs in the pelvic cavity.

“Aberrant regulation and activation of the complement system have been observed in the peritoneal cavity of women affected by endometriosis.”

Simplified: Inside the abdomen, this constant immune activation fuels inflammation, pain, and lesion growth.

6. Immune-targeted treatments may be effective.

“Complement inhibition may represent a new approach for the treatment of endometriosis.”

Simplified: Future non-hormonal therapies could calm the immune system instead of blocking hormones, offering better options for those who cannot tolerate hormonal therapy.

Summary

Endometriosis likely develops as an immune-system disorder that causes chronic inflammation, not just a hormonal imbalance. It develops when immune clearance fails and inflammation promotes lesion survival. Researchers are now investigating immune-modulating therapies, including complement and JNK-pathway inhibitors, as potential disease-modifying treatments.

Refer to the JNK Inhibitor One-Sheet in the Endo Justice bio for more information on emerging immune-pathway therapies.