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The impact of gut microbiota, inflammation and oxidative stress on endometriosis, pain, quality of life and condition of patients' health

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Abstract

Endometriosis is a chronic complex, systemic inflammatory disease which affects 5-10% of reproductive-age women. There is a need for a surgical laparoscopy to establish the correct diagnosis, which means that the disease is still underdiagnosed and leads to undertreated patients' health condition. Scientists are trying to find other factors causing and exacerbating this disease. Some of them like gut microbiome, inflammation and oxidative stress associated with endometriosis are recent discoveries.

Aim of study and materials

Aim of this article is to overview studies published on PubMed in the last 5 years. This ground is a new promising field of research and way to improve the quality of treatment in endometriosis.

State of knowledge

There is a lack of understanding of pathogenesis of endometriosis. The last scientific findings record the role of the gut microbiome in inflammatory conditions, proliferative conditions and estrogen metabolism. Other studies propose an involvement of the gut microbiome in endometriosis, this disease complications and reproductive health.

Conclusion

Endometriosis can have many forms and conditions. There are many symptoms and complications associated with this disease which are involved with a lot of questions without answers. Recently, scientists have connected many diseases with microbiota and immune dysbiosis. It revealed their probable role in development of endometriosis. This article will present the last conclusions on the subject.

Keywords: endometriosis, inflammation, oxidative stress, microbiome, gut microbiome, microbiota, chronic pelvic pain

Introduction

Endometriosis is defined as a chronic, gynaecological, proinflammatory condition characterised by endometrial-like tissue present outside of the uterus. It can lead to estrogen-driven inflammation. [1,2]. This endometrial-like tissue typically grows on or near reproductive organs like the ovaries and fallopian tubes, the exterior of the uterus, or the tissues close to the uterus and ovaries (peritoneum) [1,2]. The extent of disease can be highly variable and it may also appear on other organs within the pelvis, such as the intestines, stomach, bladder, or cervix. In uncommon cases, it can be found in other body parts like spleen, pleura, pericardium or central nervous system [2,3]. Endometriosis presents many challenges in healthcare and quality of patients' lives. This disease involves many other difficulties including demanding surgical procedures, expensive treatments and psychiatric issues (depression and anxiety) [3].

Latterly, there is an increasing understanding of the impact of microbiota dysbiosis in many diseases. Scientists examine the relationship between microbiome and diseases in distant host sites indirectly causing conditions like pregnancy complications, adverse pregnancy outcomes, polycystic ovary syndrome and cancer. It also has a role in development of endometriosis [4].

1. Endometriosis

1.1. Epidemiology

Estimates indicate that endometriosis affects 5 to 10/15% of women in reproductive age. The age of diagnosis usually ranges between 25-45 years [3,5]. Infrequently, there are some reported cases with premenarchal patients and postmenopausal women. It is difficult to determine the real prevalence of endometriosis. The estimates suggest that 5-50% infertile women, 5-21% hospitalized for pelvic pain women and 2-11% asymptomatic women have endometriosis [3]. To confirm the gravity of the problem endometriosis has been reported in 75% patients with dysmenorrhea and in 44% patients overall in this particular study [3,5].

1.2. Pathophysiology

The endometriosis development is still unclear. There are many theories and hypotheses regarding pathophysiology. Understanding these facts is crucial, forasmuch as it will help in prevention, diagnosis and treatment [6,7]. Many researches confirm the significant impact of environmental factors like dioxin pollution, radiation and oxidative stress from retrograde menstruation, genital tract and pelvic microbiome to anomalies connected with endometriosis [7].

Sampson's Theory

Theory based on retrograde menstruation. This is the most widely accepted cause of endometriosis. In this process, menstrual blood moves backward, flows through the fallopian tubes into the pelvic area and causes menstrual

tissue to be deposited in the peritoneum and growth on and into the ovary and other peritoneal organs [6]. Retrograde menstruation happens in 90% of women in their reproductive age. Studies confirm that the blood in peritoneal fluid was found in 90% of women with patent tubes by laparoscopy. Unfortunately there are some difficulties in explaining why not all women developed endometriosis [6,7].

One of the possible theories mentions that endometriosis can be caused by the decreased function of the immune system, which is not able to eliminate endometrial cells from peritoneal cavity and other ectopic places [6].

However, Sampson's theory does not explain endometriosis in adolescents before menarche, in women with Mayer–Rokitansky–Küster–Hauser syndrome and in males. Moreover, studies suggest that endometriosis cells are not specifically the same, transplanted endometrial tissue [7,8]. There are many chemical, immunologic, inflammatory processes and genetic changes which have been observed in the last 40 years. The gap between the endometriosis and retrograde menstruation highlights the presence of different/further mechanisms [8].

The coelomic metaplasia theory

Theory explains endometriosis as a result of abnormal differentiation of cells in the mesothelial lining of the peritoneum. In the embryonic phase, the coelomic epithelium is the source of the mesothelium of serous membranes and the epithelium lining of the Müllerian ducts cavity (which develop into the endometrium inside the uterine). Cells in the mesothelial lining of the peritoneum abnormally differentiate into endometrial cells along the migratory pathway of Müllerian ducts and subsequently they spread on the posterior pelvic floor (mainly in the pouch of Douglas) [8.9]. Metaplastic changes are supposed to appear as a result of inflammatory processes, hormonal influences, endogenous immunological or biochemical factors, which their origin comes from eutopic endometrial tissue. This embryological theory can explain the location of endometriosis in the pouch of Douglas, uterosacral ligaments and medial broad ligaments [8,9].

A mouse study revealed that mesenchymal stem cells from peritoneal endometriosis can contribute to the vascularization of lesions and are prone to spread to the lungs. Moreover, hypothesis is able to support the fact that endometriosis is present in rare cases like in adolescents before menarche, in human female fetuses, in women with Mayer–Rokitansky–Küster–Hauser syndrome and in men after long-term high doses of estrogens treatment (due to prostate cancer) [8,9].

Metastatic theory

This theory establishes that a tiny amount of the endometrial tissue with participation of promoters of lymphangiogenesis in endometrium - vascular endothelial growth factor-C/-D (VEGF-C/VEGF-D) regulated by proinflammatory cytokines interleukin 1β (IL-1 1β), tumour necrosis factor α (TNFα), IL-7 and CD74 might be dispersed via the uterine-draining lymph vessels throughout menstruation. This theory is predicated on a discovery of endometrial polyp which was extending into the lumen of a lymph vessel. The lymphatic capillaries are found in almost all organs thus it can explain the occurrence of endometriosis lesions in lymph nodes and distant places such as the brain, lungs, heart and eye [10].

Immunological theory

In recent years, research revealed that the condition for the development of endometrium by epithelial metaplasia or implantation of foreign antigens is local immunological tolerance. These observations have formulated an immunological theory of endometriosis [10,11]. The deviations of the immune system functioning has been observed in patients with endometriosis concern both cellular and humoral immunity at the systemic and local levels. It seems that the activity reduction of natural cytotoxic cells in the patients' blood is extremely important, because these cells participate in immunological surveillance and regulate functioning of the immune response. Approximately 80% of patients have antibodies in the IgA, IgG and IgM classes directed against endometrial and ovarian antigens. The defect of the local cellular response is expressed by an increase in total number and the activity of macrophages in the peritoneal fluid and in the fallopian tubes, proportionally to the extent of endometrial changes. They are known as a source of tumor necrosis factor-α (TNF-α) and vascular endothelial growth factor (VEGF), both of them have a potent inflammatory and angiogenic effect [10,11]. Cytokines, released from activated macrophages, increase and extend the inflammation within the peritoneum thereby the pain associated with endometriosis is escalated [11].

Genetic theory

No clear pattern of inheritance has been determined and the concept that multiple genes contribute to endometriosis is generally accepted. Research on identical twins indicates that endometriosis has an estimated total heritability of roughly 51%. Daughters of mothers with surgically diagnosed endometriosis have over double the danger of developing the disease. Further, familial inheritance of endometriosis tends to be more severe with an earlier beginning of symptoms compared to sporadic instances [30].

Overall, none are prevalent and in total these genetic variants account for just a small portion of disease risk [30].

1.3. Clinical

The clinical signs of endometriosis are numerous and various, depending on the position of the lesions. Endometriosis is widespread in the body, especially on the surface of peritoneal organs and ovarian cyst [12]. It is a systemic disease and the omnipresent symptom is pain: cyclic pelvic pain, periovulatory pain, dysmenorrhea, dyspareunia (positional or permanent), chronic non-cyclic pelvic pain, infertility, dysuria and dyschezia. Infrequently, cyclic hemoptysis, cyclic umbilical bleeding, nasal bleeding, cyclic constipation, and urinary urgency are reported by patients [12,13].

Magnetic resonance imaging MRI and transvaginal US can be valuable methods in diagnosis of endometriosis. These techniques are able to detect certain large endometriotic lesions and cysts (these are mainly recognized by the US) [14]. Another potential type of diagnostics are biomarkers. Cancer Antigen 125 CA-125 is an important indicator of epithelial cell ovarian cancer, but it can be elevated in other gynecological diseases such as endometriosis [14].

Nowadays, despite the huge development of medical imaging, interviews and physical examinations are still an effective tool. Unfortunately there are no specific symptoms and markers to diagnose endometriosis [14].

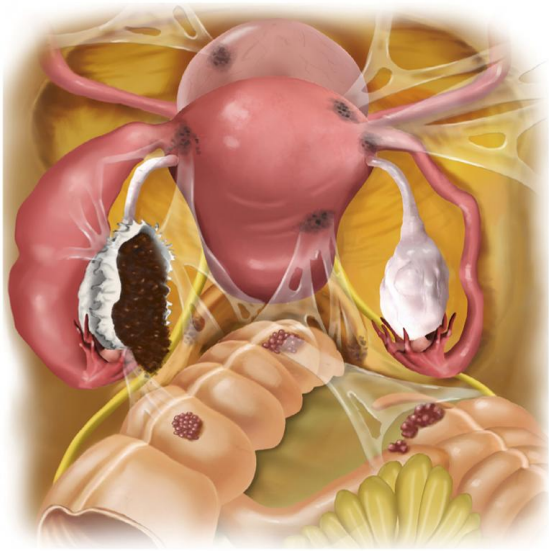
Laparoscopy is the „gold standard" for the diagnosis of endometriosis. We can visualize pathological implants which make it the most reliable and definitive method. Tissue biopsy and the pathological analysis determine the aggressiveness of the lesions [15].

1.4. Classification

Patients are categorized with the 2021 American Association of Gynecologic Laparoscopists (AAGL) and American Society for Reproductive Medicine (ASRM) and ENZIAN classification systems. AAGL and ASRM classifications are defined in a 4-point system [16,17].

American Association of Gynecologic Laparoscopists (AAGL) is a scoring system that rates the severity of endometriosis based on anatomy. It aims to improve understanding and standardize the classification of endometriosis and to aid in planning surgical treatment. The system divides endometriosis into four stages (I-IV) [16], based on a total score that reflects the complexity of surgical treatment. The AAGL scoring system takes into account the location and depth of endometrial invasion, as well as the presence of other factors such as adhesions and the presence of changes in internal organs [16]. Classification details:

Superficial	Score
< 3 cm	2
≥ 3 cm	4
Vagina (muscularis)	**Score**
< 3 cm	5
≥ 3 cm	8
Left Ovary	**Score**
Superficial	2
< 3 cm	5
≥ 3 cm	7
Left Ureter	**Score**
Extrinsic	6
Intrinsic	8
Hydroureter	9
Left Fallopian Tube	**Score**
Slight serosal involvement /damage	2
Moderate immobility	4
Severe immobility	6
Complete obstruction	7
Cul-de-sac obliteration	**Score**
Partial	6
Complete	9
Rectum/ Sigmoid colon	**Score**
< 3 cm	7
≥ 3 cm	9
Rectovaginal septum	**Score**
Present	8



Retrocervical	Score
< 3 cm	5
≥ 3 cm	8
Bladder/ detrusor	**Score**
< 3 cm	5
≥ 3 cm	7
Right Ovary	**Score**
Superficial	2
< 3 cm	5
≥ 3 cm	7
Right Ureter	**Score**
Extrinsic	6
Intrinsic	8
Hydroureter	9
Right Fallopian Tube	**Score**
Slight serosal involvement /damage	2
Moderate immobility	4
Severe immobility	6
Complete obstruction	7
Small bowel/ Cecum	**Score**
< 3 cm	6
≥ 3 cm	8
Appendix	**Score**
Present	5

AAGL Endometriosis Stage	Total Score
Stage 1	≤8
Stage 2	9 to 15
Stage 3	16 to 21
Stage 4	>21

Source: https://observatorio-api.fm.usp.br/server/api/core/bitstreams/1106c3dd-337a-4633-a1d7-adaa65914b0e/content

The ASRM (American Society for Reproductive Medicine) classification of endometriosis divides the disease into four stages, from I (minimal) to IV (severe), based on the size and location of lesions and the presence of adhesions [17].

Classification details:

Stage I (minimal): Small foci of endometriosis, usually less than 5 mm, non-vascularized adhesions in the ovaries and fallopian tubes, free fimbriae of the fallopian tubes [17].

Stage II (mild): Endometriosis foci with a diameter greater than 5 mm, adhesions between the sacrouterine ligaments and the ovaries, in the fallopian tubes and in the rectouterine pouch, endometrial cysts [17].
III degree (moderate): Adhesions of the sacrouterine ligaments with the ovaries, fallopian tubes, fimbriae of the fallopian tubes, foci in the adhesions of the ovaries and in the rectouterine pouch [17].
IV degree (severe): The most severe degree, characterized by numerous adhesions leading to deformation of the organs, lack of uterine mobility, adhesion to the intestines [17].

The ENZIAN classification is a descriptive and comprehensive classification of endometriosis that includes all aspects of the disease - peritoneal, ovarian, deep, and adhesion endometriosis. It is more detailed than traditional classification systems such as the ASRM scale. It allows for an accurate description of deep lesions and their location, which facilitates communication between physicians and understanding of what the disease looks like from the inside [17].

1.5. Treatment

Endometriosis treatment is individualized. It depends on the stage of the disease, the patient's age and her plans for motherhood. Endometriosis is treated primarily with hormonal and surgical treatment and other additional methods, such as pain medication and dietary support [18].
Treatment options:
Pain Management: over-the-counter NSAIDs like ibuprofen and naproxen or prescription pain medications can help relieve pain and inflammation by blocking the production of prostaglandins [19].
Hormonal Therapies:

- Birth Control Pills (combined estrogen and progestin pills help control the menstrual cycle and reduce pain) [19];
- Progestins (progestin-only therapies, like injections or implants, can stop menstrual periods and endometrial tissue growth, potentially relieving symptoms) [19];
- GnRH Agonists/Antagonists (these medications suppress ovulation and reduce hormone levels, slowing or stopping endometrial tissue growth) [19];
- Danazol (a synthetic androgen, danazol can shrink the displaced tissue of the uterus, providing pain relief) [19].

Surgery:

- Laparoscopy: a minimally invasive procedure where a surgeon uses a thin tube with a camera to remove or destroy endometrial tissue, remove cysts, and address adhesions [18,20];
- Laparotomy: a more invasive open surgery, typically reserved for cases where laparoscopy is not feasible [18,20];
- Hysterectomy: removal of the uterus, a definitive treatment option for some [18,20];
- Oophorectomy: removal of the ovaries, often performed in conjunction with a hysterectomy, can provide long-term pain relief [18,20].

It's important to understand that endometriosis is not curable. Treatments aim to manage symptoms and improve quality of life. Endometriosis can affect fertility. Treatment may focus on reducing pain and improving fertility outcomes, potentially including assisted reproductive technologies. The best treatment approach will vary based on the severity of symptoms, desire for pregnancy, and other individual factors [18,19,20].

2.1. The gut microbiota

The role of microorganisms living in close partnership with human hosts is significant, researching constantly and still not fully understood. These micro partners are estimated to be 10-100 trillion and they are called our „last organ". The complex of microbes are referred to as the „microbiota" and their genes together are „microbiome". Human intestinal tract is dominated by bacteria of the phylum Bacteroidetes and Firmicutes (representing up to 90% of gut microbiota), Proteobacteria, Actinobacteria, Verrucomicrobia and Fusobacteria [26,28].

Bacteroidetes mainly contain Bacteroides and Prevotella. Firmicutes are largely represented by Bacillus, Lactobacillus, Clostridium, Enterococcus, and Ruminococcus. Proteobacteria involve Desulfovibrio and Escherichia. Less numerous classes such as Actinobacteria is represented by Bifidobacterium and Verrucomicrobia by Akkermansia spp [26,28].

Gut microbiome is responsible for many functions: synthesis of micronutrients; metabolism of carbohydrates complex; regulation of signaling pathways; produce short chain fatty acids (SCFAs), anti-inflammatory lipids; regulation and release of gut hormones (peptide YY, glucagon-like peptide-1, cholecystokinin). Gut commensals maintain the intestinal epithelium integrity and ward off bacterial invasion. They produce and secrete a wide range of bioactive molecules which provide the immunomodulatory and antimicrobial action [26].

2.2. The gut microbiota and endometriosis

Endometriosis, a condition where tissue similar to the uterine lining grows outside the uterus, is increasingly linked to alterations in the gut microbiota. Studies have shown that individuals with endometriosis exhibit reduced diversity in their gut microbial composition, along with imbalances and an increase in pathogenic bacteria. These changes in the gut microbiome can disrupt immune function, contribute to inflammation, and potentially exacerbate gastrointestinal symptoms [28,29].

Endometriosis is thought to be closely connected to immune disorders because its traits are alike to those of autoimmune conditions like reduced apoptosis, elevated cytokine levels and atypical cell-mediated pathways. Many researchers have performed detailed studies on the connection between endometriosis and the gut microbiota [28,29].

2.3. Gut Microbiota Alterations in Endometriosis

Dysbiosis of the gut microbiota:

Recent studies have revealed that individuals with endometriosis often have a less diverse gut microbiome compared to healthy patients. These alterations can disrupt immune function, elevate inflammation, and contribute

to the long-term inflammatory condition observed in endometriosis. Furthermore, dysregulation of gut permeability may additionally exacerbate gastrointestinal symptoms in afflicted individuals [21].

Research has shown that the Firmicutes/Bacteroidetes ratio was increased after successful modeling of endometriosis in rats, indicating that endometriosis causes a gut microbiota imbalance. Firmicutes was the major type of microbiota in endometriosis' patients, Bacteroidetes was second the most abundant phylum [21].

Additionally, the abundances of Cyanobacteria, Acidobacteria, Fusobacteria, Saccharibacteria and Actinobacteria were significantly increased in patients with endometriosis [21,26]. Specifically, they discovered reduced amount of Ruminococcus, Clostridia and Lachnospiraceae. These commensals produce SCFAs which increase intestinal integrity and are involved in several other gut–microbiome dysbiosis like Crohn's disease. Hormonal treatment of endometriosis revealed the growth of Ruminococcus bacterial class and other SCFAs producers. Contrarily, Prevotella (from Bacteroidetes group) was found in high abundance in endometriosis patients and it has connection with gastrointestinal symptoms - bloating, vomiting, nausea and flatulence [26].

Gut microbiota and estrogen:

Estrogen is an important hormone which maintains a reproductive female system and regulates the microenvironment of the female lower genital tract. However, disturbed estrogen balance may be a cause of proliferative diseases such as endometrial cancer, hysteromyoma, endometriosis by stimulating the proliferation of female genital epithelial cells [21,22].

The gut microbiota (including Bifidobacterium, Bacteroid, Lactobacillus and Escherichia coli) can produce β-glucosidase and β-glucuronidase. These enzymes accelerate and increase the estrogen degradation and in sequence intensifie the reabsorption of free estrogen and improves its' level in the circulation [21,22,24]. Notably, studies have demonstrated a substantial rise of Escherichia coli levels in the feces of patients with endometriosis. These results indicate that the gut flora could contribute to increased estrogen amounts, producing a setting that encourages the advancement of endometriosis [22,24].

Finally, it seems that gut microbial β-glucuronidase - gmGUS can become a potential biomarker which can be used to early diagnosis of diseases caused by disturbed estrogen balance [23].

Gut microbiota and inflammation

Endometriosis development is closely related to estrogen. However, studies have shown that the growth of ectopic lesions is continued even in ovariectomized animals. This observation indicates that the innate immune system in the pelvic cavity can also cause the development of ectopic lesions, excluding the influence of ovarian steroids. Studies demonstrate that the inflammatory microenvironment is linked to the development of endometriosis. Endotoxin and lipopolysaccharide from foreign gram-negative bacteria can activate the macrophages and dendritic cells [21,22]. The inflammatory reaction is the crucial process in the progression of endometriosis, resulting in pain, tissue remodeling, fibrosis, adhesion development and infertility. Increased levels of pro-inflammatory agents, anti-inflammatory factors and immune cells reflect a disturbance in the regulation of inflammation and anti-inflammatory processes, in addition to alterations in intestinal microbiota, intestinal permeability and other immune regulatory processes [22].

In the peritoneal fluid are present inflammatory factors, cytokines and chemokines. The levels of factors IL-1β, IL-18, and TGF-β are also increased in peritoneal cavity. The immune system unable to effectively restrain the inflammation may lead to increased pro inflammatory factors. It can cause difficulties in clearing ectopic endometrial tissue and growth pathological lesions. Dysregulation of pro-inflammatory and anti-inflammatory processes reflects the changes in intestinal microbiota, intestinal permeability and other immune processes [21,22]. Some recent studies have shown that the gut microbiota may incorrectly affect ectopic endometrial lesions and peritoneal fluid content. Patients with endometriosis reveal increased numbers of Escherichia coli and Shigella - gut bacteria. It is connected with increased levels of lipopolysaccharide - LPS (endotoxin, an amphiphilic integral component of the outer cell membrane of Gram-negative bacteria) in the gut and serum. LPS with secondary inflammatory mediators participate in the development of endometriosis [21,22].

2.4. Probiotics in endometriosis

The gut microbiota can be separated into symbiotic bacteria, pathogenic bacteria and probiotics. Gut microbiota disorder is closely related to a reduction in the amount of probiotics within the body. A few researches have revealed that the addition of probiotics correct and restore the microbiota imbalance, therefore it became a potential therapeutic factor for various diseases (including endometriosis - non-surgical treatment option).
The gut microbiota regulation can be achieved through different strategies - dietary intervention with specific nutrients, probiotics, fecal bacteria transplantation [22].

Endometriosis patients demonstrated increased production of pro-inflammatory cytokines IL-1 and IL-6 by peripheral blood mononuclear cells (PBMCs) compared to individuals without endometriosis. A study investigated the effect of supplementing the Lactobacillus acidophilus on PBMCs. The findings suggest that after 48 hours this probiotic effect on bacterial cells exhibited modulatory properties, leading to a reduction in cytokines IL-1 and IL-6 production. It suggests potential therapeutic benefits for endometriosis [22,25].

In another randomized placebo-controlled trial, concerning women with stage 3 and 4 endometriosis, LactoFem (containing Lactobacillus formula) was investigated orally once a day during the 8 weeks. 37 participants, without the hormonal treatment through the last 3 weeks, were assessed for pain severity (using Visual Analogue Scale - VAS) for dyspareunia, dysmenorrhea and chronic pelvic pain. Results were collected at baseline, after 8 weeks and after 12 weeks intervention. Findings presented that The Lactobacilli had beneficial effects on pain, especially on dysmenorrhea and chronic pelvic pain after 8 weeks of treatment, which suggest that the supplementation may have a positive impact on endometriosis-related pain symptoms [22,25].

Studies with mice participation were investigating the oral supplementation of Lactobacillus. Endometriosis dysregulates cytokines activity, disturbs immune reaction and increases the inflammation, which can lead to impaired NK cells activity and intensify pathological changes. Trial demonstrated that probiotics increase IL-6, IL-12 concentration, promote Natural Killer (NK) cell activity which reverse this immune dysregulation, reduce endometriotic lesions and prevent the growth of lesions in rats. These trials confirm potential beneficial effects of probiotics supplementation [22,25].

2.5. Fecal microbiota transplantation

Fecal microbiota transplantation (FMT) - a standardized treatment, which involves feces transplantation of healthy people into the gastrointestinal tract of patients with dysbacteriosis for reconstruction of the gut microbiota and treat disease [21,27]. Actually, FMT is used for the treatment of gastrointestinal diseases, chronic hepatitis B, metabolic syndrome, drug-resistant bacterial infections, neuropsychiatric diseases and others.

Currently, trials have shown that FMT might be used for treating female reproductive tract illnesses. Regarding the effectiveness of FMT in endometriosis, studies demonstrated that endometriotic mice that received transplants of feces from healthy mice displayed diminished lesion expansion compared to those transplanted with feces from endometriotic mice. These initial investigations highlight the potential of FMT in lessening endometriosis through strengthening of barrier integrity. FMT may be used as an additional treatment of this yet incurable condition [21,26].

Each subsequent study increases the role of gut microbiota of endometriosis development, consequently FMT can be the next, innovative treatment option [21,27].

Conclusion

Despite the fact that the two fields are not greatly connected, a consistent trend of evidence of a gut microbiome–endometriosis relationship is disclosed by recent studies. Most significantly, a diminished gut microbiome diversity and an increased Firmicutes/Bacteroidetes ratio have chiefly been connected to increased endometriosis risk.

Decreased populations of Ruminococcus, Clostridia and Lachnospiraceae and elevated abundances of Bifidobacterium, Cyanobacteria, Acidobacteria, Fusobacteria, Saccharibacteria and Actinobacteria and Enterobacteriaceae, primarily Escherichia/Shigella, at the genus level are reported alterations in gut microbiota of patients.

Fecal microbiota transfers from endometriotic mice to healthy cohorts encourage lesion growth, confirming the role of gut commensals in disease development.

It is significant to recremember that microbial inhabitants of the gut dwell in intricate communities, communicating and interacting with one another and with the gut's epithelial cells. This knowledge presents substantial opportunities to mitigate the endometriosis via adjustment of the gut microbiome, interactions and related metabolites. Specifically, identifying bacterial prospects that promote or safeguard against endometriosis in reproductive-aged women will expedite efforts to diagnose, prevent, and treat endometriosis.

Concurrently, the gut microbiota can be altered through antibiotics, fecal microbiota transfer, probiotics, hormonal medicaments, nutrients and other methods to act in endometriosis.

Despite the limitations, the exploration of the connection between endometriosis and the gut microbiome offers significant promise for further research. Additional investigation in this domain could provide valuable insights into the complex interaction between these elements and offer novel pathways for enhancing our comprehension and management of endometriosis.

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Author's contribution

Conceptualization - Anna Hanslik;

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Visualization - Agata Białek, Monika Klimczak;

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References

1. Hugh S Taylor, Alexander M Kotlyar, Valerie A Flores; https://pubmed.ncbi.nlm.nih.gov/33640070/; DOI: 10.1016/S0140-6736(21)00389-5

2. Catherine Allaire, Mohamed A Bedaiwy, Paul J Yong; https://pubmed.ncbi.nlm.nih.gov/36918177/; DOI: 10.1503/cmaj.220637

3. Gabriela Cano-Herrera, Sylvia Salmun Nehmad, Jimena Ruiz de Chávez Gascón, Amairani Méndez Vionet, Ximena A van Tienhoven, María Fernanda Osorio Martínez, Mauricio Muleiro Alvarez, Mariana Ximena Vasco Rivero, María Fernanda López Torres, María Jimena Barroso Valverde, Isabel Noemi Torres, Alexa Cruz Olascoaga, Maria Fernanda Bautista Gonzalez, José Antonio Sarkis Nehme, Ignacio Vélez Rodrígun, Eder Gabriel

Rivera Rosas, Dante Carbajal Ocampo, Ramiro Cabrera Carranco; https://pubmed.ncbi.nlm.nih.gov/39062050/; DOI: 10.3390/biomedicines12071476

4. Jim Manos; https://pubmed.ncbi.nlm.nih.gov/35393656/; DOI: 10.1111/apm.13225

5. Hanne Van Gestel, Celine Bafort, Christel Meuleman, Carla Tomassetti, Arne Vanhie; https://pubmed.ncbi.nlm.nih.gov/38943813/; DOI: 10.1016/j.rbmo.2024.103848

6. Maria Ariadna Ochoa Bernal, Asgerally T Fazleabas; https://pubmed.ncbi.nlm.nih.gov/38892003/; DOI: 10.3390/ijms25115815

7. Philippe R Koninckx, Rodrigo Fernandes, Anastasia Ussia, Larissa Schindler, Arnaud Wattiez, Shaima Al-Suwaidi, Bedayah Amro, Basma Al-Maamari, Zeinab Hakim, Muna Tahlak; https://pubmed.ncbi.nlm.nih.gov/34899597/; DOI: 10.3389/fendo.2021.745548

8. Teresa Mira Gruber, Sylvia Mechsner; https://pubmed.ncbi.nlm.nih.gov/34205040/; DOI: 10.3390/cells10061381

9. K Matsuura, H Ohtake, H Katabuchi, H Okamura; https://pubmed.ncbi.nlm.nih.gov/10087424/; DOI: 10.1159/000052855

10. Jelizaveta Lamceva, Romans Uljanovs, Ilze Strumfa; https://pubmed.ncbi.nlm.nih.gov/36901685/; DOI: 10.3390/ijms24054254

11. Teresa Mira Gruber, Sylvia Mechsner; https://pubmed.ncbi.nlm.nih.gov/34205040/; DOI: 10.3390/cells10061381

12. Sanjay K Agarwal, Charles Chapron, Linda C Giudice, Marc R Laufer, Nicholas Leyland, Stacey A Missmer, Sukhbir S Singh, Hugh S Taylor; https://pubmed.ncbi.nlm.nih.gov/30625295/; DOI: 10.1016/j.ajog.2018.12.039

13. Edgardo Rolla; https://pubmed.ncbi.nlm.nih.gov/31069056/; DOI: 10.12688/f1000research.14817.1

14. Hafiz Muhammad Arsalan, Hina Mumtaz, Antonio Simone Lagana; https://pubmed.ncbi.nlm.nih.gov/40185537/; DOI: 10.1016/bs.acc.2025.01.004

15. Elma Pašalić, Murtaza M Tambuwala, Altijana Hromić-Jahjefendić; https://pubmed.ncbi.nlm.nih.gov/37844487/; DOI: 10.1016/j.prp.2023.154847

16. Mauricio S Abrao, Marina Paula Andres, Charles E Miller, Julian A Gingold, Mariona Rius, Joao Siufi Neto, Francisco Carmona; https://pubmed.ncbi.nlm.nih.gov/34583009/; DOI: 10.1016/j.jmig.2021.09.709

17. Jörg Keckstein, Gernot Hudelist; https://pubmed.ncbi.nlm.nih.gov/33558167/; DOI: 10.1016/j.bpobgyn.2020.11.004

18. Giulia Bonavina, Hugh S Taylor; https://pubmed.ncbi.nlm.nih.gov/36387918/; DOI: 10.3389/fendo.2022.1020827

19. Patricia Ribeiro de Carvalho França, Anna Carolina Pereira Lontra, Patricia Dias Fernandes; https://pubmed.ncbi.nlm.nih.gov/35807280/; DOI: 10.3390/molecules27134034

20. Matthew Latham Macer, Hugh S Taylor; https://pubmed.ncbi.nlm.nih.gov/23182559/; DOI: 10.1016/j.ogc.2012.10.002

21. Rui Qin, Gengren Tian, Junbao Liu, Lu Cao; https://pubmed.ncbi.nlm.nih.gov/36506023/; DOI: 10.3389/fcimb.2022.1069557

22. Anjeza Xholli, Francesca Cremonini, Isabella Perugi, Ambrogio Pietro Londero, Angelo Cagnacci; https://pubmed.ncbi.nlm.nih.gov/38139822/; DOI: 10.3390/ph16121696

23. Shiwan Hu, Qiyou Ding, Wei Zhang, Mengjiao Kang, Jing Ma, Linhua Zhao; https://pubmed.ncbi.nlm.nih.gov/37559394/; DOI: 10.1080/19490976.2023.2236749

24. Isabella Weber, Anna Sienko, Aleksandra Urban, Carolyn Szwed, Krzysztof Czajkowski, Pawel Basta, Jacek Sienko; https://pubmed.ncbi.nlm.nih.gov/37772919/; DOI: 10.5603/gpl.97581

25. Meng-Yao Wang, Li-Xuan Sang, Si-Yu Sun; https://pubmed.ncbi.nlm.nih.gov/38617735/; DOI: 10.3748/wjg.v30.i12.1655

26. Chandni Talwar, Vertika Singh, Ramakrishna Kommagani; https://pubmed.ncbi.nlm.nih.gov/35878972/; DOI: 10.1093/biolre/ioac147

27. Gianluca Quaranta, Maurizio Sanguinetti, Luca Masucci; https://pubmed.ncbi.nlm.nih.gov/31827467/; DOI: 10.3389/fimmu.2019.02653

28. Mary E Salliss, Leslie V Farland, Nichole D Mahnert, Melissa M Herbst-Kralovetz; https://pubmed.ncbi.nlm.nih.gov/34718567/; DOI: 10.1093/humupd/dmab035

29. Tamy Colonetti, Maria Carolina Saggioratto, Antonio José Grande, Laura Colonetti, João Carlos Denoni Junior, Luciane Bisognin Ceretta, Leonardo Roever, Fábio Rosa Silva, Maria Inês da Rosa; https://pubmed.ncbi.nlm.nih.gov/38601772/; DOI: 10.1155/2023/2675966

30. Philippe R Koninckx, Anastasia Ussia, Leila Adamyan, Arnaud Wattiez, Victor Gomel, Dan C Martin; https://pubmed.ncbi.nlm.nih.gov/30527836/; DOI: 10.1016/j.fertnstert.2018.10.013