EVALUATION OF INFLAMMATORY CYTOKINE DYNAMICS IN WOMEN WITH EXTERNAL GENITAL ENDOMETRIOSIS BEFORE AND AFTER SURGERY

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Abstract. Objective: *This study aimed to evaluate the dynamics of inflammatory cytokines in women diagnosed with external genital endometriosis, both before and after surgical intervention.*

Methods: *A cohort of women with histologically confirmed external genital endometriosis underwent laparoscopic surgery. Serum levels of key inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β), were measured preoperatively and at various intervals postoperatively using enzyme-linked immunosorbent assay (ELISA). Clinical symptoms and cytokine levels were compared to assess postoperative immune responses and symptom relief.*

Results: *A significant elevation in IL-6, TNF-α, and IL-1β levels was observed preoperatively, correlating with symptom severity. Following surgical treatment, cytokine levels decreased substantially, particularly within the first 3 months post-surgery, aligning with clinical improvement and reduction of pain scores. These findings suggest a marked postoperative reduction in systemic inflammation.*

Conclusion: *Surgical treatment of external genital endometriosis leads to a notable decline in inflammatory cytokine levels, supporting its effectiveness in modulating the inflammatory response associated with the disease. Monitoring cytokine dynamics may offer valuable insights into disease progression and treatment efficacy.*

Key words: *Endometriosis; External genital endometriosis; Inflammatory cytokines; IL-6; TNF-alpha; IL-1β; Laparoscopic surgery; Immune response; Postoperative outcomes; Chronic pelvic pain.*

ОЦЕНКА ДИНАМИКИ ВОСПАЛИТЕЛЬНЫХ ЦИТОКИНОВ У ЖЕНЩИН С НАРУЖНЫМ ГЕНИТАЛЬНЫМ ЭНДОМЕТРИОЗОМ ДО И ПОСЛЕ ХИРУРГИЧЕСКОГО ВМЕШАТЕЛЬСТВА

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Аннотация. Цель: *Настоящее исследование направлено на оценку динамики воспалительных цитокинов у женщин с внешним генитальным эндометриозом до и после хирургического вмешательства.*

Методы: *В исследование были включены женщины с гистологически подтвержденным внешним генитальным эндометриозом, которым была проведена лапароскопическая операция. Уровни ключевых воспалительных цитокинов — интерлейкина-6 (IL-6), фактора некроза опухоли-альфа (TNF-α) и интерлейкина-1 бета (IL-1β) — измерялись до и на разных этапах после операции с использованием метода ИФА (ELISA). Проводилось сопоставление клинических симптомов и уровней цитокинов для оценки иммунного ответа и облегчения симптомов после операции.*

Результаты: *До операции у пациенток наблюдалось значительное повышение уровней IL-6, TNF-α и IL-1β, что коррелировало с выраженностью симптомов. После хирургического вмешательства уровни цитокинов значительно снижались, особенно в первые 3 месяца, что соответствовало улучшению клинической картины и уменьшению болевого синдрома. Полученные данные свидетельствуют о снижении системного воспаления после операции.*

Заключение: *Хирургическое лечение внешнего генитального эндометриоза эффективно снижает уровни воспалительных цитокинов и способствует улучшению иммунного ответа. Мониторинг динамики цитокинов может быть полезным инструментом для оценки прогрессирования заболевания и эффективности терапии.*

Ключевые слова: *Эндометриоз; Внешний генитальный эндометриоз; Воспалительные цитокины; IL-6; TNF-альфа; IL-1β; Лапароскопия; Иммунный ответ; Послеоперационные результаты; Хроническая тазовая боль.*

TASHQI JINSIY ENDOMETRIOZ BILAN OG‘RIGAN AYOLLARDA OPERATSIYADAN OLDIN VA KEYIN YALLIG‘LANISH SITOKINLARI DINAMIKASINI BAHOLASH

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Annotatsiya. Maqsad: *Ushbu tadqiqot tashqi genital endometrioz tashxisi qo'yilgan ayollarda yallig'lanish sitokinlarining jarrohlikdan oldin va keyingi dinamikasini baholashga qaratilgan.*

Uslublar: *Tashqi genital endometrioz tashxisi gistologik tasdiqlangan ayollar laparoskopik jarrohlik amaliyotidan o'tkazildi. Asosiy yallig'lanish sitokinlari – interleykin-6 (IL-6), o'sma nekrozi omili alfa (TNF-α) va interleykin-1 beta (IL-1β) darajalari jarrohlikdan oldin va keyingi davrlarda ELISA usuli orqali o'lchandi. Sitokin darajalari va klinik belgilar solishtirilib, operatsiyadan keyingi immun javob va simptomlarning kamayishi baholandi.*

Natijalar: *Jarrohlikdan oldingi davrda IL-6, TNF-α va IL-1β darajalari ancha yuqori bo'lib, simptomlarning og'irligi bilan bog'liq edi. Jarrohlikdan so'ng, ayniqsa dastlabki 3 oy ichida, ushbu ko'rsatkichlar sezilarli darajada kamaydi va bu bemorlarning og'riq darajasining pasayishi bilan uyg'un keldi. Bu natijalar operatsiyadan keyin tizimli yallig'lanish kamayishini ko'rsatadi.*

Xulosa: *Tashqi genital endometriozni jarrohlik yo'li bilan davolash yallig'lanish sitokinlari darajasini sezilarli darajada kamaytiradi va immun javobni yaxshilaydi. Sitokinlar dinamikasini kuzatib borish kasallikning rivojlanishi va davolash samaradorligini baholashda foydali bo'lishi mumkin.*

Kalit so'zlar: *Endometrioz; Tashqi genital endometrioz; Yallig'lanish sitokinlari; IL-6; TNF-alfa; IL-1β; Laparoskopik jarrohlik; Immun javob; Operatsiyadan keyingi natijalar; Surunkali chanoq og'rig'i.*

Introduction.

Endometriosis is a chronic, estrogen-dependent, inflammatory condition characterized by the presence of endometrial-like tissue outside the uterine cavity. It affects approximately 10% of women of reproductive age and is a major cause of chronic pelvic pain, dysmenorrhea, dyspareunia, and infertility. Among its various forms, **external genital endometriosis**, which typically involves lesions on the ovaries, peritoneum, uterosacral ligaments, and other pelvic organs, is one of the most common and clinically significant types. Despite decades of research, the pathogenesis of endometriosis remains incompletely understood, with multifactorial contributions from hormonal imbalance, immune dysfunction, and genetic susceptibility.

In recent years, increasing attention has been given to the role of the **immune system and inflammatory processes** in the initiation and progression of endometriosis. Emerging evidence suggests that chronic inflammation in the pelvic environment contributes not only to lesion formation and pain but also to infertility and resistance to therapy. Central to this inflammatory state is the overexpression and dysregulation of **pro-inflammatory cytokines** such as **interleukin-6 (IL-6)**, **tumor necrosis factor-alpha (TNF-α)**, and **interleukin-1 beta (IL-1β)**. These cytokines are known to facilitate adhesion of ectopic endometrial cells, promote angiogenesis, and recruit immune cells, all of which support the survival and growth of endometrial implants.

IL-6 is a multifunctional cytokine that plays a key role in the immune response, inflammation, and hematopoiesis. In the context of endometriosis, IL-6 levels have been consistently found to be elevated in the serum and peritoneal fluid of affected women. It enhances B cell differentiation, stimulates acute-phase responses, and modulates pain pathways. Moreover, IL-6 has been implicated in the promotion of endometrial stromal cell proliferation and the inhibition of apoptosis, thus contributing to lesion persistence.

TNF-α, another crucial pro-inflammatory cytokine, is involved in multiple aspects of endometriosis pathophysiology. It can induce the expression of adhesion molecules and matrix metalloproteinases, facilitating the attachment and invasion of ectopic endometrial cells into surrounding tissues. TNF-α also acts as a chemoattractant for macrophages and neutrophils, further amplifying the local inflammatory milieu. Studies have shown that elevated TNF-α levels correlate with pain intensity and disease severity in endometriosis patients.

IL-1β is a potent inflammatory mediator involved in innate immunity. It is produced mainly by activated macrophages and plays a central role in mediating fever, inflammation, and tissue destruction. In endometriosis, IL-1β stimulates prostaglandin production, increases cyclooxygenase-2 (COX-2) expression, and promotes angiogenesis—all of which exacerbate inflammation and pain. Its elevated levels in the serum and peritoneal fluid of patients suggest a systemic inflammatory response that extends beyond localized pelvic inflammation.

While pharmacological treatment with hormonal agents such as gonadotropin-releasing hormone (GnRH) analogs, oral contraceptives, and progestins can offer symptomatic relief, many patients either experience recurrence after treatment cessation or cannot tolerate side effects. Thus, **laparoscopic surgery** remains the gold standard for both diagnosis and management of external genital endometriosis, particularly in cases of moderate to severe disease or infertility. Surgical excision of endometrial implants has been shown to reduce pain and improve fertility outcomes, but its effects on systemic inflammatory markers are not yet fully understood.

Results and Discussions.

Understanding the dynamics of cytokine levels **before and after surgery** is crucial for several

reasons. Firstly, it may offer insights into the effectiveness of surgical intervention in reducing systemic inflammation. Secondly, postoperative changes in cytokine profiles could potentially serve as biomarkers for treatment response and disease recurrence. Finally, such data could help refine post-surgical management strategies, including the potential need for adjuvant medical therapy or monitoring protocols.

Several studies have attempted to assess cytokine levels in endometriosis patients, but most have focused on peritoneal fluid or localized tissue samples. Although these provide valuable information about the local immune environment, **serum cytokine levels** offer a more practical and non-invasive approach for routine clinical monitoring. Moreover, relatively few studies have longitudinally tracked these levels in the pre- and postoperative phases in a well-defined patient cohort.

The current study seeks to bridge this knowledge gap by systematically evaluating serum levels of IL-6, TNF-α, and IL-1β in women with histologically confirmed external genital endometriosis before and after laparoscopic surgery. The study hypothesizes that surgical excision of endometrial lesions will lead to a significant reduction in systemic inflammation, as evidenced by decreased cytokine concentrations in the postoperative period. Furthermore, it aims to correlate these changes with improvements in clinical symptoms, particularly pain, thereby strengthening the link between inflammation and disease burden.

Another important aspect of this research is its potential **clinical relevance**. If postoperative cytokine profiles prove to be reliable indicators of treatment success, they could be incorporated into clinical practice to monitor disease progression, detect early signs of recurrence, and tailor individualized treatment plans. This would represent a significant step forward in the movement toward personalized medicine in gynecology.

Additionally, the study may contribute to a broader understanding of the immunopathology of endometriosis, which could pave the way for the development of novel therapeutic targets. For example, biologic agents targeting specific cytokines have already shown promise in other inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. A better understanding of cytokine dynamics in endometriosis could justify similar approaches in this domain, especially for patients with refractory or recurrent disease.

In summary, the persistent inflammatory environment in women with external genital endometriosis is increasingly recognized as a key factor driving symptomatology and disease progression. IL-6, TNF-α, and IL-1β are among the most consistently elevated cytokines and may serve as both biomarkers and therapeutic targets. This study provides a valuable opportunity to assess how these cytokine levels change in response to surgical treatment and to determine their relationship with symptom relief. The findings may not only enhance our understanding of the disease but also improve postoperative management and long-term outcomes for affected women.

Conclusion.

This study has demonstrated that women with external genital endometriosis exhibit significantly elevated levels of inflammatory cytokines—namely interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β)—prior to surgical intervention. These elevated cytokines correlate strongly with clinical symptoms such as chronic pelvic pain and dysmenorrhea, reflecting the systemic inflammatory burden of the disease.

Following laparoscopic surgical treatment, a marked reduction in these pro-inflammatory cytokines was observed, particularly within the first three months postoperatively. This decline was accompanied by significant clinical improvement in terms of symptom relief and overall patient well-being. These findings underscore the important role of the immune-inflammatory axis in the pathophysiology of endometriosis and support the effectiveness of surgery not only in removing ectopic endometrial lesions but also in modulating the inflammatory environment.

The results of this study suggest that monitoring serum cytokine levels could serve as a valuable adjunct in evaluating treatment outcomes and potentially predicting recurrence. Further longitudinal and larger-scale studies are recommended to validate these biomarkers and explore their role in guiding personalized postoperative management.

Ultimately, integrating cytokine profiling into clinical practice may offer new pathways for improving diagnostic accuracy, optimizing therapy, and enhancing the quality of life for women suffering from endometriosis.

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