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Anti-Inflammatory Nutrition in the Prevention and Management of Endometriosis: Implications for Physical Performance and Quality of Life

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Abstract

Introduction and purpose of the work. Endometriosis is a chronic, oestrogen-dependent disease with a complex aetiopathogenesis and a multidimensional clinical presentation, characterised by the presence of active endometrioid glands and stromal tissue located outside the uterine cavity. The diagnosis of endometriosis remains challenging and requires a multidisciplinary approach encompassing physical examination, imaging techniques, and, when necessary, laparoscopy. Current approaches to the treatment of endometriosis are generally classified into three principal categories: pharmacological, non-pharmacological, and surgical interventions. Endometriosis is an inflammatory disease; therefore, any factors affecting immune system regulation may influence its onset, symptom severity and progression. This literature review aims to evaluate the influence of dietary factors on the risk of endometriosis development and on the severity and presentation of its clinical symptoms.

Materials and methods. A comprehensive literature search was conducted in the Google Scholar data base up to 1995 and PubMed up to data base. The review included clinical control studies, cross-sectional studies, prospective cohort studies, and randomised studies.

Summary. Current evidence indicates that diets rich in anti-inflammatory components may substantially reduce the risk of endometriosis and mitigate the severity of associated symptoms. Nevertheless, further research is required to elucidate the specific mechanisms and the extent to which individual dietary components influence the progression of the disease.

Keywords: endometriosis diet, anti-inflammatory diet, healthy lifestyle, quality of life, inflammatory disease, dyslipidaemia

1. Introduction:

Endometriosis is a chronic, oestrogen-dependent disease with a complex aetiopathogenesis and a multidimensional clinical presentation, characterised by the presence of active endometrioid glands and stromal tissue located outside the uterine cavity. [1] Its symptomatology includes pelvic pain, abdominal pain with symptoms that may mimic irritable bowel syndrome, menstrual disorders, dyspareunia and infertility. [2] Based on various sources, the prevalence of this disease ranges from 6% to approximately 10% of women of reproductive age, which does not exclude the onset of the disease in adolescence. [3] The diagnosis of endometriosis is a complex process and often fraught with diagnostic difficulties. [4] Contemporary clinical guidelines demonstrate a progressive transition from laparoscopy as the initial diagnostic modality toward advanced imaging techniques, including magnetic resonance imaging and transvaginal ultrasonography, which in many cases constitute essential tools augmenting the overall clinical assessment. [5]

2. Epidemiology:

Endometriosis is estimated to affect approximately 10% of women of reproductive age. [6] The prevalence of the disease is thought to range from 2–11% among asymptomatic women, 5–50% among women experiencing infertility, and 5–21% among those hospitalised for pelvic pain. [7] Furthermore, epidemiological data indicate that endometriosis may be present in 49–75% of adolescents reporting chronic pelvic pain. [8]

Endometriosis is a gynaecological condition in which pelvic and abdominal pain represents one of the most common clinical manifestations, frequently occurring also during sexual activity.

[6] This symptomatology contributes to a significantly reduced quality of life, both physically and psychologically, which may, in selected cases, be improved through surgical intervention. [9]

3. Pathophysiology:

Endometriosis is regarded as one of the most debilitating female disorders in contemporary medicine. It is characterised by the presence of endometrial tissue outside its normal location in the uterine cavity. [6] The disorder can be classified into three subtypes based on histopathology and anatomical location: superficial endometriosis, deep infiltrating endometriosis (DIE), and ovarian endometriotic cysts. [11] It is a well-documented fact that, under normal circumstances, the menstrual cycle is accompanied by the process of exfoliation of the endometrial layer. This process is subject to regulation by the female hormonal system. It is important to note that endometrial tissue located outside the confines of the uterine cavity is incapable of undergoing this specific process. Furthermore, the growth of this tissue is contingent upon the presence of oestrogen hormones. [12]

There are number of theories that seek to explain the aetiology of endometriosis. Among the most widely examined are retrograde menstruation, extrauterine-sourced stem cells, hematogenous or lymphatic spread, coelomic metaplasia and Müllerian rest induction. [11,13]

Retrograde menstruation

Sampson's theory, known as retrograde menstruation theory, has been around for decades. This theory focuses on the assumption that menstrual blood containing exfoliated endometrial cells flows backwards through the patent fallopian tubes into the peritoneal cavity, where endometrial cells are then implanted. The process of angiogenesis, as initiated by peritoneal macrophages, has been demonstrated to be a crucial factor in the stimulation of the growth and development of endometrial lesions. This theory provides a comprehensive explanation for only two forms of endometriosis, namely ovarian and superficial peritoneal endometriosis. However, it does not address the phenomenon of deep infiltrating and extraperitoneal endometriosis, leaving this aspect of the condition unexplained. [10]

Immune dysregulation

Inflammatory diseases such as endometriosis can be explained by dysregulation of the immune system, represented by macrophages, neutrophils, NK cells, dendritic cells and T cells. Macrophages, responsible for the process of phagocytosis of pathogens, are antigen-presenting cells for T cell activation. The number of these cells is subject to regulation according to the menstrual cycle, with the highest values being attained during the proliferative phase of the endometrium. As previously mentioned, in the context of endometriosis, the number of macrophages increases in all phases of the menstrual cycle and does not undergo changes. Furthermore, the reduced expression of CD3, CD36 and annexin A2 has been demonstrated to result in impaired phagocytosis and incomplete endometrial shedding. The release of pro-inflammatory cytokines, including TNF α , IL-6, IL-8 and IL-1 β , by peritoneal macrophages results in inflammation and the development of endometrial lesions. Another inflammatory mechanism involves the increased local production of chemotactic factors, such as IL-8, ENA-78, and HNP1-3, by epithelial cells, which leads to the recruitment of neutrophils into the peritoneal cavity. Conversely, the cytotoxic function of NK cells is inhibited by IL-6, IL-15, and TGF- β , resulting in their accumulation within the peritoneal cavity. Another salient aspect pertains to the imbalance between Th1 and Th2 lymphocytes, with a predominance of the latter, which are responsible for suppressing both cellular and humoral immune responses. Increased expression of IL-10 and IL-12 has been demonstrated to contribute to the weakening of Th1-mediated cellular immunity, and the number of Th1 cells remains reduced in endometriosis. These observations suggest that the inflammatory process plays a pivotal role in the pathogenesis of endometriosis and its severity. [10]

4. Diagnosis:

The diagnosis of endometriosis remains challenging and requires a multidisciplinary approach encompassing physical examination, imaging techniques, and, when necessary, laparoscopy. [6] Clinical suspicion is primarily based on the presence and severity of symptoms. Ultrasound and magnetic resonance imaging constitute the preferred diagnostic modalities for ovarian endometriomas and deep infiltrating endometriosis. [14] In contrast, the diagnosis of superficial endometriosis necessitates laparoscopy—an intervention which, according to the guidelines of the Polish Society of Gynaecologists and Obstetricians, should be performed with the intention of implementing pharmacological treatment as an adjunct rather than as a substitute for diagnostic procedures.

According to the most recent guidelines issued by the Polish Society of Gynaecologists and Obstetricians, transvaginal ultrasound is recommended as the first-line imaging modality in patients with suspected endometriosis. Subsequently, when symptoms and ultrasound findings indicate a high likelihood of deep infiltrating endometriosis, a targeted ultrasound assessment following an endometriosis-specific algorithm or pelvic magnetic resonance imaging employing the same algorithm is advised. Conversely, negative imaging findings do not exclude the presence of superficial peritoneal lesions. Among the available diagnostic markers, CA 125 has been identified as a potential adjunct in the diagnostic process; however, its utility remains limited, serving only as a supplementary indicator rather than a definitive diagnostic tool. [15]

5. Treatment:

The management of endometriosis constitutes a complex and iterative process that requires ongoing assessment of the patient, encompassing both the therapeutic efficacy of the chosen intervention and the potential development of adverse effects. [16] The selection of an optimal treatment strategy depends on multiple factors, including the clinical presentation, the severity and character of symptoms, and the individual needs and expectations of the patient. In cases involving infertility, patient-specific priorities assume particular importance in guiding clinical decision-making. [6] Current approaches to the treatment of endometriosis are generally classified into three principal categories: pharmacological, non-pharmacological, and surgical interventions. [17] Among these, surgical management is frequently regarded as the only modality capable of achieving definitive therapeutic benefit. [18] Pharmacological treatment includes a broad spectrum of agents, such as non-steroidal anti-inflammatory drugs, progestogens, and antiprogestogens (e.g., medroxyprogesterone acetate, norethisterone acetate, dienogest, desogestrel, and gestrinone). Additional options comprise gonadotropin-releasing hormone analogues—both agonists and antagonists—as well as aromatase inhibitors. [19] Surgical management typically involves laparoscopy as the primary operative approach, although laparotomy may be required in selected clinical circumstances. [18]

Dyslipidaemia in Endometriosis

Endometriosis is an inflammatory disease; therefore, any factors affecting immune system regulation may influence its onset, symptom severity and progression. It has been established that a dietary regime comprising unprocessed foods, abundant in vitamins, green vegetables,

and healthy fats, exerts an influence on hormone balance and, consequently, this oestrogen-dependent disease.

As demonstrated by a cross-sectional study from NHANES (1999–2006) and a bidirectional Mendelian randomisation study, there is a correlation between elevated triglyceride levels and an increased risk of developing endometriosis. The present study investigates the expression of vascular cell adhesion molecule-1 (VCAM-1) and E-selectin in endometrial glands. These molecules, acting as mediators of inflammatory processes, are known to be induced by elevated triglyceride concentrations. Furthermore, it has been reported that women with stage III and IV endometriosis exhibit significantly elevated levels of E-selectin. [20]

A cross-sectional analysis of the NHANES dataset from 1999 to 2006 revealed an association between the non-HDL/HDL cholesterol ratio (NHHR) and the risk of endometriosis among individuals who consume alcohol. In these individuals, elevated non-HDL cholesterol levels and impaired antioxidant activity of HDL-C contribute to enhanced oxidative stress, lipid peroxidation, and inflammatory responses, manifesting as dyslipidaemia. This study provides novel insight into the potential development of endometriosis in women with elevated NHHR values, particularly those who consume alcohol. [21]

A cross-sectional study was conducted among 2,224 women with confirmed endometriosis, utilising data from the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2006. The findings indicated a correlation between elevated cardiometabolic index (CMI) values and the development of endometriosis. The CMI, calculated using the formula $\text{triglycerides (TG) / high-density lipoprotein cholesterol (HDL-C)} \times \text{WHtR}$ (waist-to-height ratio, $\text{WHtR} = \text{waist circumference} / \text{height}$), has been demonstrated to correlate with increased dyslipidaemia and obesity. Therefore, the CMI may serve as a marker for the development of endometriosis. [22]

Diet in Endometriosis

In view of the established correlation between elevated lipid metabolism indicators and the risk of developing endometriosis, a number of studies have been undertaken to evaluate the influence of diet on the progression of the disease and the manifestation and severity of individual symptoms. [6]

A cross-sectional study based on data from the 2001-2006 NHANES survey analysed 4,149 women, 287 of whom reported endometriosis. The objective of the present study was to analyse the relationship between the Dietary Inflammatory Index (DII) and the risk of endometriosis.

The results of the study indicated a positive correlation between a higher DII value, indicative of a pro-inflammatory diet, and an increased risk of endometriosis. Furthermore, the relationship was significantly influenced by higher alcohol and caffeine consumption and lower dietary fibre and vitamin C intake. As is well established, vitamin C is a potent antioxidant that mitigates oxidative stress, while dietary fibre influences the diversity of the gut microbiota, thereby reducing intestinal permeability and the development of inflammation. The results of the study align with other research that has found a link between higher consumption of red meat and trans fats, components of a pro-inflammatory diet, and an increased risk of endometriosis. [23]

A further case-control study was conducted between April 2015 and March 2016 at two referral centres, namely the Royan Institute and the Vali-Asr Reproductive Health Research Centre in Tehran, Iran. The study analysed data from 207 women diagnosed with endometriosis and 206 women without the disease, who served as the control group. The data were collected using a questionnaire that assessed demographic and reproductive characteristics, as well as dietary habits. The subjects reported the frequency of consumption of a selected range of food products during the week preceding the interview. The study indicated that a higher intake of green vegetables and fresh fruit may reduce the risk of endometriosis. It is noteworthy that the authors observed a correlation between the consumption of 4–6 servings of red meat per week and a reduced risk of the disease. This finding is at odds with the results of other studies, in which red meat – which is generally regarded as a component of a pro-inflammatory diet – was linked to an increased risk of endometriosis. In addition, an elevated consumption of dairy products, incorporating three to five servings of cheese weekly, was correlated with a diminished likelihood of developing the condition. This protective effect may be explained by the ability of dairy products to decrease levels of interleukin-6 (IL-6) and tumour necrosis factor- α receptor 2 (TNF- α R2), inflammatory markers implicated in the development and progression of inflammatory diseases. In addition, calcium and vitamin D, which are naturally present in dairy products, have been shown to reduce concentrations of insulin-like growth factor I (IGF-1), a known promoter of cellular proliferation, and to increase levels of transforming growth factor β (TGF- β), which plays a role in mitigating oxidative stress. [24]

A case-control study was conducted in Tehran, Iran, between February and September 2021, on 115 women diagnosed with endometriosis and 230 healthy women. The objective of the study was to assess the association between adherence to the Mediterranean diet and the Healthy

Diet Indicator (HDI) and the odds of developing endometriosis among Iranian women. The dietary intake of the participants was evaluated using the Food Frequency Questionnaire (FFQ-24), a validated food album, and the Medi-Lite score to determine adherence to the Mediterranean dietary pattern. The overall quality of diet was assessed using the Healthy Diet Indicator, a tool that takes into account the intake of saturated and unsaturated fatty acids, protein, carbohydrates, fibre, fruits and vegetables, legumes, nuts and seeds, as well as cholesterol. The analysis was based on data from 105 women diagnosed with endometriosis and 208 healthy controls. A significant disparity was observed in Medi-Lite scores between healthy women and women afflicted with endometriosis, with the former demonstrating considerably higher scores. Furthermore, it was observed that women whose Medi-Lite scores exceeded the population average were 94% less likely to develop endometriosis than those with lower adherence. A reduced risk of endometriosis was associated with higher consumption of fruits, nuts, vegetables, fish, and legumes, as well as with lower intake of dairy products and meat. Conversely, HDI scores were found to be lower among women with endometriosis, and women with higher HDI scores were 95% less likely to develop the disease. A correlation has been demonstrated between a reduced risk of endometriosis and increased fibre intake, as well as reduced consumption of trans fats and monounsaturated fatty acids (MUFAs). These findings are consistent with evidence indicating that components of the Mediterranean diet mitigate inflammation—partly through their influence on IL-6, IL-16, and IL-32—and that its high magnesium content helps prevent increases in intracellular calcium, exerting a relaxing effect on uterine smooth muscle and consequently reducing pain. [25]

A prospective cohort study was conducted as a pilot project at the Máxima Medical Centre, a teaching hospital in Veldhoven, the Netherlands, between 2020 and 2023. The study involved 47 women and aimed to investigate the effect of a low-FODMAP diet on intestinal symptoms, such as constipation and bloating, as well as on pain and quality of life in patients with endometriosis. The intervention entailed a 4-week elimination phase, during which participants were instructed to refrain from consuming FODMAP-rich foods. This was followed by a 10-week period of gradual reintroduction, during which the participants were advised to reintroduce FODMAP-rich foods into their diet in a controlled manner. The most frequently excluded FODMAP components were fructooligosaccharides and lactose. Of the women who met the inclusion criteria, 34 initiated the diet and 24 completed the full intervention. Following the conclusion of the dietary protocol, enhancements were evident across all primary domains of the EHP-30 questionnaire, including the domains of "work life" and "sexual relations", in

comparison with the initial baseline scores. Among participants who completed the intervention, 84% reported a reduction in intestinal symptoms, 53% noted a decrease in bloating, and 65% experienced reduced pain, particularly chronic pelvic pain. These findings provide robust evidence to support the hypothesis that the low-FODMAP diet exerts a beneficial effect on the presence and severity of symptoms in patients diagnosed with endometriosis. [26]

Conclusions:

The impact of endometriosis on health is extensive, encompassing the digestive system, the mental state of patients, and numerous other aspects of health. [6] The management of this condition is often challenging and intricate; however, a comprehensive review of extant research findings suggests that dietary habits may have a significant impact on the manifestation of symptoms and the risk of developing the disease. [23] Research has demonstrated that a diet abundant in green vegetables and fruit, nuts, legumes and olive oil, characteristic elements of the Mediterranean diet, significantly reduces the risk of endometriosis. [23,25]

Concurrent observations have indicated that elevated alcohol consumption, caffeine intake, and trans fat augmentation may be associated with an augmented risk of developing the disease. [23] A beneficial effect on symptom severity has also been reported with a low-FODMAP diet, which eliminates highly fermentable foods, including lactose, the main component of dairy products. [26] The results of these studies are consistent with the aetiopathogenesis of endometriosis, in which immune system dysregulation plays a key role. [6] The elimination of dietary elements that have been demonstrated to exacerbate inflammation, by increasing the concentration of inflammatory markers and factors that activate oxidative stress, may represent a significant component of a strategy aimed at reducing the risk of disease development. [23,25] Further research is required to ascertain whether a diet that is anti-inflammatory and all of its constituent elements reliably leads to a decrease in the likelihood of developing endometriosis. [6,23]

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