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Anti-inflammatory effect of the Mediterranean diet in women with endometriosis: a literature review

Efecto antiinflamatorio de la dieta mediterránea en mujeres con endometriosis: una revisión bibliográfica

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Abstract: Endometriosis is a chronic gynecological disease that affects many women and presents symptoms such as dysmenorrhea, dyspareunia and infertility, which interfere with quality of life, damaging physical and mental health, as well as social and intimate relationships. Therefore, changing eating habits, with the adoption of diets rich in anti-inflammatory compounds and like the Mediterranean pattern, can interfere with the pathophysiological processes of the disease, such as inflammation, metabolism and hormone activity. Therefore, the main objective of this research is to investigate evidence on the anti-inflammatory effect of the Mediterranean diet as a therapeutic approach in the context of endometriosis. To this end, this study consists of a complete literature analysis related to the topic addressed, using the PubMed (US National Library of Medicine) databases. Applying the descriptors in Health Science (DeCs): Mediterranean diet, anti-inflammatory diet, endometriosis and nutrition. For the inclusion criteria, complete articles published in the last 5 years, written in Portuguese and English, were selected. Regarding the results, it was verified that the different nutrient modifiers present in the Mediterranean diet provide anti-inflammatory effects that reduce pain, control hormones and improve the quality of life of women diagnosed with endometriosis. However, given the results obtained, the Mediterranean diet presents promising results in combating pain and inflammatory processes, and can be used as a nutritional strategy for the treatment and prevention of endometriosis.
Keywords: Mediterranean diet; Anti-inflammatory diet; Endometriosis; Nutrition.

Resumen: La endometriosis es una enfermedad ginecológica crónica que afecta a muchas mujeres y presenta síntomas como dismenorrea, dispareunia e infertilidad, que interfieren en la calidad de vida, perjudicando la salud física y mental, así como las relaciones sociales e íntimas. Por ello, el cambio de hábitos alimentarios, con la adopción de dietas ricas en compuestos antiinflamatorios y similares al patrón mediterráneo, puede interferir en los procesos fisiopatológicos de la enfermedad, como la inflamación, el metabolismo y la actividad hormonal. Por lo tanto, el objetivo principal de esta investigación es investigar la evidencia sobre el efecto antiinflamatorio de la dieta mediterránea como enfoque terapéutico en el contexto de la endometriosis. Para ello, este estudio consiste en un completo análisis bibliográfico relacionado con el tema abordado, utilizando las bases de datos PubMed (US National Library of Medicine).

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Aplicando los descriptores en Ciencias de la Salud (DeCs): Dieta mediterránea, dieta antiinflamatoria, endometriosis y nutrición. Para los criterios de inclusión, se seleccionaron artículos completos publicados en los últimos 5 años, escritos en portugués e inglés. En cuanto a los resultados, se comprobó que los diferentes modificadores de nutrientes presentes en la dieta mediterránea proporcionan efectos antiinflamatorios que reducen el dolor, controlan las hormonas y mejoran la calidad de vida de las mujeres diagnosticadas de endometriosis. Sin embargo, dados los resultados obtenidos, la dieta mediterránea presenta resultados prometedores en la lucha contra el dolor y los procesos inflamatorios, y puede utilizarse como estrategia nutricional para el tratamiento y la prevención de la endometriosis.
Palabras clave: *Dieta mediterránea; Dieta antiinflamatoria; Endometriosis; Nutrición.*

INTRODUCTION

Endometriosis is characterized by the growth of tissue identical to the endometrium outside the uterus. It is a chronic gynecological disease that affects 176 million women worldwide, which represents around 5 to 10% of women of reproductive age (Zondervan *et al*., 2018). Patients suffering from endometriosis have a series of alterations in the body, forming an inflammatory microenvironment and causing a variety of lesions that can affect everything from the peritoneum, ovaries and fallopian tubes to the bladder and intestines (Rogers *et al.,* 2016).

This pathology can be divided according to the degree of development and location of the lesions, the pelvic area and the diameter of the cysts: Superficial, ovarian and deep endometriosis (Koninckx *et al.*, 2021*). In* addition, symptoms such as pelvic pain, dysmenorrhea, dyspareunia and even infertility are recurrent, which can negatively impact physical and emotional health, to represent a burden on the patient's quality of life and productivity (As-Sanie *et al.,* 2019*).* Despite the high incidence, the cause of endometriosis is still poorly understood. Hormonal, immunological and neurological factors participate in the mechanisms that favor the onset of symptoms. Diagnostic errors are frequent, and therapies have limited efficacy, with a high rate of symptom recurrence (Liu *et al.,* 2023).

Diet is one of the main modifiable risk factors, both in the origin and progression of endometriosis, as well as in the presence of pain symptoms, increased lesions and infertility. The effect of diet on endometriosis can be explained by hormonal changes in estrogen, prostaglandin metabolism, inflammation or pelvic muscle contractility (Nodler *et al.,* 2020). The Mediterranean dietary pattern is currently considered one of the best in the world. Based on the food cultures of the ancient civilizations that developed in the Mediterranean basin, this diet is composed of vegetables, rich in antioxidants and unsaturated fat, which has been strongly associated with lower rates of non-communicable diseases and mortality (Scoditti; Tumolo; Garbarino, 2022).

Clinical trials and mechanistic studies have shown that some of the physiological and pathological processes related to the disease, such as inflammation, estrogenic activity, the menstrual cycle and prostaglandin metabolism, can be influenced by the Mediterranean diet (Karlsson; Patel; Premberg, 2020).

Red meat, for example, decreases the protein that affects hormonal functions (SHBG) and accumulates estradiol levels (Yamamoto *et al.,* 2018). The varied consumption of phytochemical fruits and vegetables can support the functions of the immune system and fight free radicals (Youseflu *et al.,* 2020). In addition, adopting the Mediterranean dietary pattern may represent a future long-term non-pharmacological therapeutic intervention to reduce cardiovascular risk in women with endometriosis and thus prevent age-related chronic diseases and improve quality of life, making it a valuable medical tool in the contemporary world (Cirillo *et al*., 2023).

Thus, the general objective of this research is to highlight studies on this subject that are considered relevant for future therapeutic interventions around women's health, especially endometriosis. A proper understanding of the disease is linked to successful diagnosis and early treatment, including through the Mediterranean diet, which offers a simple dietary pattern rich in antioxidant and anti-inflammatory compounds capable of modulating the hormonal and metabolic activity of the pathophysiological processes of endometriosis, making it a strong modifiable factor for the disease.

THEORETICAL BACKGROUND

Pathophysiology of endometriosis

Endometriosis is a recurring pathology that can have a significant impact on women's lives, resulting in pain, infertility, decreased quality of life and an impact on routine, relationships and livelihoods. Despite this, its pathophysiology and epidemiology are still poorly understood, allowing for some hypotheses and alternative therapies (Agarwal *et al.,* 2019).

The first theory concerns retrograde menstruation, described by Sampson in the 1920s, and is one of the main explanations for endometriosis. According to the author, during the follicular phase of the menstrual cycle, oestrogen and progesterone levels become dysregulated, unlike what happens in the normal menstrual cycle, when hormone levels drop and the endometrium is eliminated in the form of bleeding, a "reflux" movement occurs, causing the endometrium to return to the abdominal cavity instead of following the vaginal canal. This results in the accumulation of endometrial cells that can spread and become implanted on the peritoneal surfaces, reaching other organs and affecting their functioning (Amro *et al*., 2022).

The Genetic-Epigenetic (GE) theory, on the other hand, describes endometriosis as a series of DNA transformations in an endometrial, stem or bone marrow cell that do not alter its sequence, but impair its functions, such as resistance to progesterone and the activity of aromatase - the enzyme that converts progesterone into estrogen - which maintains control of estrogen levels in the ovaries. The excessive growth

of clones of cells 'identical' to the endometrium outside the uterine cavity provokes a chronic inflammatory response, causing lesions associated with the formation of new blood vessels by pre-existing vessels (angiogenesis), bleeding and immunological alterations until the tissue heals (fibrosis), resulting in irregularities (Koninckx *et al*., 2021). The predisposition to genetic cell defects at birth explains the greater tendency to endometriosis and infertility throughout life. The risk increases after puberty, due to the onset of menstruation and sexual activity, which can deregulate estrogen levels and gradually decrease with the onset of menopause (Amro *et al*., 2022).

Endometriosis is classified into three types: Superficial pelvic, which is characterized by the growth of tissue in the peritoneum, the membrane that covers the walls of the abdominal and pelvic cavity, protecting all the organs and structures in this region, presenting minor lesions that can lead to delayed diagnosis and progression of the disease; Cystic ovarian, as the name implies, is associated with the presence of tissues in the ovary or cysts (endometriomas), occurring mainly in the reproductive phase of women and; Deep endometriosis, which is defined as a lesion that can penetrate the extraperitoneal space and invade various pelvic organs, such as the bladder, large intestine, ureters and vagina, with a depth of up to 5mm (Souza; Fontenele; Vargens, 2022).

Although they are clonal and microscopically similar, endometriosis lesions have different clinical characteristics. In most women, the symptoms of the disease are non-specific, since endometriosis needs to grow for a few years before becoming symptomatic and can easily be confused with other gynecological and gastrointestinal diseases (Surrey *et al*., 2020). Currently, the average time between the onset of symptoms mentioned by patients and the decisive diagnosis is approximately 7 years. Patients with long delays in diagnosis had a higher clinical burden, worsening of symptoms and comorbidities associated with endometriosis, as well as having higher economic costs due to the use of recurrent health resources compared to women diagnosed earlier (Soliman *et al*., 2018).

The diagnosis of superficial pelvic endometriosis requires laparoscopy, which should be conducted according to the patient's history, clinical examination and symptoms. This is an obstacle, as it is often avoided and postponed, especially in younger women, as surgery can be unexpectedly difficult to perform. Ultrasound or magnetic resonance imaging are the most suitable methods for diagnosing cystic and deep endometriosis. However, clinical and imaging tests are not enough to detect smaller, superficial lesions, and laparoscopy is the best alternative for suspected endometriosis. Given that, many lesions are not identified and around 30% of normal-looking appendages harbor endometriosis (Mabrouk *et al*., 2020).

Endometriosis needs more attention when it comes to diagnosis, as delay can favor the progression of the disease and the formation of adhesions that can impair fertility and aggravate the risk of central and pelvic sensitization (Lee *et al*., 2020). Information on pathological factors differs according to the specialist,

and not everyone has a complete understanding of pathophysiology, genetics, treatment, diet and lifestyle (Porpora *et al.,* 2013).

Medical treatment options include painkillers, hormonal treatments and surgical intervention to remove the lesions or remove the uterus. However, like medication, surgery is not always effective and is linked to clinically relevant risks (Becker *et al.,* 2017). This failure is attributed to the complexity of each case and, to date, none of the treatments have managed to cure the disease and symptoms reappear as soon as medication is stopped (Brichant *et al.,* 2021). Thus, while the search for new treatment options continues, the therapeutic benefits of food have been investigated with the aim of collaborating with treatment and improving quality of life in women.

The Role of the Mediterranean Diet in Endometriosis

The Mediterranean Diet (MD), proposed by Ancel Keys, is linked to the dietary pattern of the civilizations that inhabited the Hellenic peninsula, Italy and the other countries in the areas surrounding the Mediterranean Sea, around the 1950s (Serra-Majem *et al*., 2019). The diet is based on a simple diet, containing a wide variety of minimally processed whole grains, vegetables with high energy reserves, legumes, seeds and nuts (Tosti; Bertozzi; Fontana, 2018). After the industrial revolution and the exaggerated consumption of processed foods, the Mediterranean diet model was removed from the current dietary pattern and there was a significant change in the population's lifestyle, increasing the incidence of cancer and chronic diseases, which was extremely low in these countries (Serra-Majem *et al*., 2020).

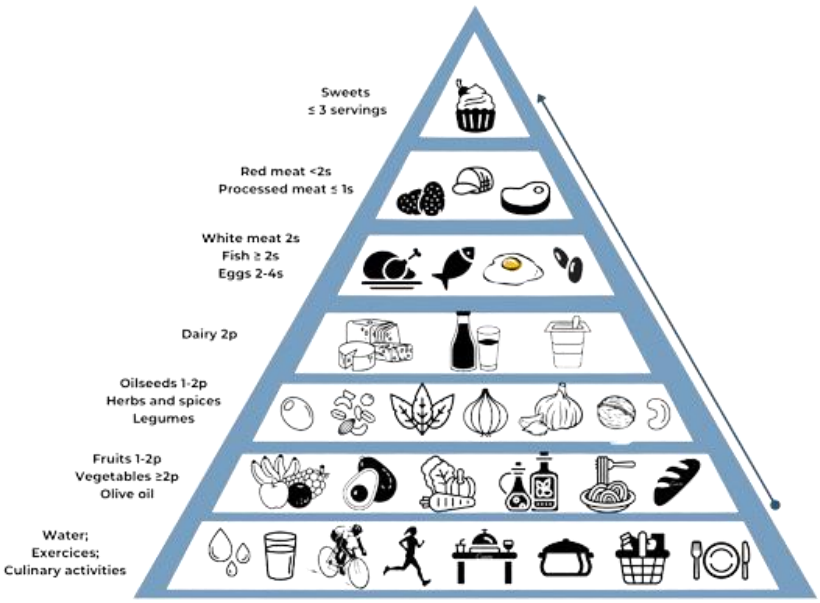
The Mediterranean diet has been shaped over the years, from the customs inherited by its ancestors at the dawn of civilization, to the present day, with the presence of industrialized foods. Various ingredients and recipes have been implemented, but with the initial idea of keeping the local tradition firm. At that time, red meat was rarely eaten, milk was rarely used, sugar and potatoes were consumed with caution. The foods regularly consumed were extra virgin olive oil (used as the main source of fat), vegetables (cereals, legumes, pulses and seeds), fruit, fish and local cheese, as well as a moderate intake of red wine during meals (Lăcătușu *et al*., 2019).

Today, this dietary model still arouses the interest of various health professionals about its benefits for the proper functioning of the body. The overall results show strong evidence attributed to specific nutrients, food components, behavior, dietary pattern and various health conditions, such as: Diabetes mellitus, neurodegenerative diseases, respiratory diseases and healthy aging (Dinu *et al*., 2018). The main explanation for these qualities can be attributed to the abundance of antioxidant and anti-inflammatory molecules in their individual foods. One hypothesis suggests that the cellular redox state may play a relevant role in modulating enzyme systems linked to antioxidant capacity. In addition, nutrients can regulate gene

expression and protein synthesis (Tsigalou *et al.*, 2020).

The Mediterranean diet, compared to other 'healthy' diets, allows a high intake of fat, if it is from virgin olive oil, nuts and oily fish, and moderate consumption of red wine during meals (Gea *et al.*, 2014). Dietary pattern analysis becomes more useful because it replaces the idea of attributing all health effects to a single food by examining the effects of the multiple interaction of nutrients in the diet. In this way, no single food principle can be used as the sole explanation for the benefits brought about by the Mediterranean diet in its entirety (Lăcătușu *et al.*, 2019). The new Mediterranean diet pyramid (Figure 01), recommended by the Mediterranean Diet Foundation, provides daily dietary guidelines for selecting foods, indicating the proportions and frequency of consumption of the main food groups to follow a healthy and balanced routine (Davis *et al.*, 2015). The standard includes all the food groups, with a variety of foods and cooking techniques, as well as adequate frequency and quantity to minimize the possibility of nutritional deficiencies. At the base, the foods that should sustain the diet and offer the most calories, and at the higher levels, foods to be consumed in moderate quantities, such as sugars and fats that should be consumed on special occasions. In addition, physical activity, rest, culinary recipes and socializing during meals are part of the Mediterranean lifestyle.

FIGURE 01: Pyramid of the Mediterranean diet.



SOURCE: Davis *et al.*, 2015.

METHODOLOGY

This is a literature review of an exploratory nature, with data collected through an electronic search

in the PubMed medical information databases between August and October 2023.

The following Health Sciences Descriptors (DeCS) were used for the searches: Mediterranean diet, endometriosis, anti-inflammatory diet and nutrition, using the Boolean expression "AND" to combine two or more keywords. The inclusion criteria were academic studies published in Portuguese or English in the last five years.

We included original studies available *online,* in full and with the central theme of the influence of the Mediterranean diet and its components on endometriosis symptoms, with a focus on the anti-inflammatory process. Studies that were not appropriate to the topic, repeated in the database and more than five (5) years old were excluded. In addition, course completion papers, dissertations and theses were also excluded. The titles and abstracts were evaluated independently, and those chosen met the proposed objective and were sent for critical reading of the complete work to compose the research results. For each study, information was extracted on publication data, population characteristics, type of dietary intervention, results and limitations.

RESULTS AND DISCUSSION

When searching the database, 97 papers were found, 05 of which reported findings on dietary factors that are part of the Mediterranean diet and are related to the condition of endometriosis; these articles were retrieved for a thorough analysis. Most of the studies were cross-sectional (Cirillo *et al.*, 2023), (Mazza *et al., 2023*), (Molina et *al.,* 2023) a qualitative study (Karlsson; Patel; Premberg, 2020) and an exploratory observational study (Krabbenborg *et al.,* 2021). A total of 2 Italian (Cirillo *et al.,* 2023), (Mazza *et al., 2023),* one in Spain (Molina *et al.,* 2023), one in Sweden (Karlsson; Patel; Premberg, 2020) and one in the Netherlands (Krabbenborg *et al.,* 2021), as shown in Table 01. Information on food intake was collected through food questionnaires in 3 studies. While 1 of them was conducted using *online* forms, the other was conducted using a forum.

TABLE 01: Studies related to the anti-inflammatory effect of the Mediterranean diet in women with endometriosis.

Author, year	Purpose of the article	Main findings
Cirillo *et al.*, 2023	To analyze the influence of dietary changes according to the Mediterranean diet on the perception of pain in endometriosis and its	There was a significant reduction in pain in terms of dyspareunia, non-menstrual pelvic pain and dysuria, as well as an improvement in bowel habits and greater adherence to the diet. In addition, the women saw an improvement in oxidative

	relationship with oxidative stress.	parameters, which cause inflammatory processes in the body.
Mazza *et al*., 2023	To evaluate the influence of dietary patterns on the relief of endometriosis symptoms.	The study revealed a significant change in eating habits and patients reported that avoiding or adding certain foods relieved their endometriosis symptoms. However, more in-depth results are needed to assess how diets impact symptoms and improve daily life.
Molina *et al.*, 2023	To identify the role of the Mediterranean diet in the endometrial metabolome and infertility.	The Mediterranean diet pattern has been shown to increase essential fatty acids, which act on the body's homeostasis and contribute to the maturation and quality of the embryo, as well as reducing levels of inflammatory factors by reducing carnitine.
Karlsson; Patel; Premberg, 2020	Exploring the symptoms of endometriosis after dietary changes.	The participants experienced an increase in well-being and a reduction in symptoms after making dietary changes, such as reducing gluten, dairy and some carbohydrates, and adding fruit, vegetables, fish and omega 3. In addition, they also reported increased energy levels and greater understanding of their bodies, a reduction in gastrointestinal discomfort and other symptoms such as headaches, nausea and allergies.
Krabbenborg *et al.*, 2021	To analyze the effects of dietary changes on endometriosis.	Patients reported an improvement in symptoms after specific adjustments to dietary interventions, such as the removal of gluten, dairy or soy, as well as the addition of vegetables, fruits and fats that are part of the Mediterranean diet. However, more in-depth evidence is needed to prove the specific effects of the diet.

SOURCE: Authors' data (2023).

In an Italian study by Cirillo *et al.* (2023) 90 Caucasian women with endometriosis diagnosed by laparoscopy and/or diagnostic imaging were evaluated during the period from March 2020 to December 2022. At the start of the study, all the women were on estrogen-progestogen therapy, and out of a total of 35 women of reproductive age included in the study, all completed the first phase and only 26 finished the study. On the tenth day after the first visit, a questionnaire was administered to assess adherence to the Mediterranean diet. The vitamin profile, oxidative stress markers, cardiovascular risk factors, anthropometric parameters and pain scale were monitored throughout the study.

The patients showed high adherence to the diet over the 6-month period. In addition, there was an increase in the consumption of fruit, vegetables and cereals, from a low to a moderate percentage. About meat, adherence was also higher over the three-month period, due to the greater consumption of white meat, as reported by the patients. Fish, on the other hand, accounted for 17.1% of patients, who said they did not increase their consumption due to taste or cost and, finally, extra virgin olive oil was consumed regularly by 100% of those surveyed since their first consultation. About the patients' vitamin profile, there was a significant increase in B12, folate and zinc, which are found in abundance in the blood.

In addition to the dietary changes, the patients had reduced pain in relation to dyspareunia, non-menstrual pelvic pain, dysuria and dyschezia, with a significant reduction over 6 months, and improved oxidative stress parameters compared to a population of healthy women of the same age. In addition, due to the high amount of fiber present in the diet, there were changes in the regularity and consistency of the stools, with a significant improvement of 35% over three months, which contributed to the women's bowel habits.

Another cross-sectional study, conducted by Mazza *et al.* (2023), an anonymous national *online* survey was conducted based on Google Forms, between April 9 and June 27, with Italian women over the age of 18, diagnosed with endometriosis at different stages. The survey aimed to investigate eating habits and the impact of the disease's symptoms on patients' daily lives. It included 4,078 participants, most of whom were between 36 and 45 years old, and 37% of whom had a severe stage of the disease. The participants were instructed to choose one of several dietary interventions, of which 7.1% opted for the Mediterranean diet.

The study showed that women with severe-stage endometriosis appear to follow the anti-inflammatory diet more often, while reducing foods rich in saturated fats and simple sugars. These findings indicate a greater attempt to control the inflammation associated with the severe stage of the disease. In addition, the women changed their eating habits, with an increase in the consumption of vegetables, fruit, cereals, legumes and fish, while dairy products, soy-based foods and foods high in saturated fats were reduced. Patients reported that avoiding or limiting certain nutrients and adding fruits and vegetables helped

relieve symptoms, due to the antioxidant effects, fiber content and magnesium present in the Mediterranean diet, which have positive effects on pelvic pain and inflammation. These dietary changes have been shown to be an adaptive response to the severity of symptoms or the progression of endometriosis, even without objective measurement of pain in the participants (Fernandes *et al.,* 2020).

(2023), 45 women from infertile couples were recruited from the Reproductive Unit between March 2019 and April 2021. Among the causes of infertility, 13 of them had endometriosis, diagnosed by laparotomy or laparoscopic surgery. The participants completed a questionnaire about their lifestyle and demographic characteristics. Their BMI was estimated, and the day of ovulation was determined by a digital ovulation test to determine infertility. In addition, endometrial tissue samples were collected and stored until analysis. For adherence to the Mediterranean diet, the MEDAS questionnaire was used, which contained 12 questions related to eating habits specific to the Mediterranean diet. The participants were categorized according to their adherence to the diet; approximately 25 of them showed high adherence, among them 07 had endometriosis.

As a result, women who were unable to have children because of endometriosis had lower levels of PUFAS, such as linoleic acid and a-linolenic acid, which are essential fatty acids present in high quantities in Western diets. These lipids play a fundamental role in body homeostasis and are considered crucial for reproductive health, contributing to embryo maturation and quality (Yang *et al.,* 2022). Greater adherence to the diet also showed lower levels of carnitine, which suggests that the diet may protect against endometriosis, since high levels of carnitines are associated with beta-oxidation dysfunction, which causes inflammatory factors (Molina *et al.,* 2023).

The findings of these studies show a relationship between pain relief and the anti-inflammatory potential of the Mediterranean diet. This can be explained by the various mechanisms of interaction between the nutrients that make up the Mediterranean pattern, especially fish, mono- and polyunsaturated fats such as omega-3, which are present in abundance. According to the study by Akyol *et al.* (2016), it was found that omega-3 polyunsaturated fatty acids (PUFA) have a regressive effect, reducing the growth of the endometrium outside the uterus and peritoneal fluid. The results of the study by Molina *et al.* (2023), revealed that women with endometriosis have low PUFA levels compared to healthy women, which can have a negative impact on endometrial functions. PUFAs have a major impact on the production of cytokines, which have the role of regulating the activity of cells in the body, and prostaglandins, lipid compounds that produce hormone-like effects. In addition, they are responsible for participating in cell membrane structures, which increases membrane fluidity (Parazzini *et al.,* 2013).

Another important factor that can influence the results of pain reduction is the increased consumption of fiber among women. This can be explained by better regulation of intestinal transit time,

which helps to control excess estrogen through fecal excretion, while at the same time decreasing the production of prostaglandins responsible for the proliferation of the disease (Cirillo *et al.,* 2023). About vitamins, the study by Santanan *et al.* (2013) found that women with pelvic pain and endometriosis showed a significant reduction in inflammatory indicators in the peritoneal fluid compared to those who did not take vitamins. In the study by Cirillo *et al.* (2023), due to changes in the Mediterranean diet, patients showed an increase in blood levels of vitamins, which contributed to an improvement in pain symptoms.

Furthermore, greater adherence to the Mediterranean diet seems to be associated with egg quality, which differed between women with different infertility diagnoses. This may be linked to the levels of different fatty acids, xanthine metabolites, carnitines and progestin steroids (Molina *et al.,* 2023). In addition, with greater adherence to the Mediterranean diet, there was a greater number of bacteroidetes and bifidobacteria, which have fermentative characteristics and modulate the intestinal system in a beneficial way (Cirillo *et al*., 2023). These results are consistent with the study by Pagliai *et al.* (2019), in which the authors found that after adhering to the Mediterranean diet for three months, the patients showed a significant change in the composition of the intestinal microbiome.

A qualitative study by Karlsson, Patel and Premberg (2020) included 50 participants aged between 18 and 45 on three Swedish endometriosis support forums on the internet between November 2016 and June 2017. The participants in this study made individual dietary changes as a form of complementary therapy, which involved increasing or decreasing the intake of different types of food in the routine. Most of the participants excluded or decreased gluten, dairy products and carbohydrates, which are foods considered stressful for the body and affect estrogen levels or inflammatory processes (Piecuch *et al.,* 2022). As a result, the participants reported that with the beneficial effects of dietary changes, there was also interest in making other lifestyle changes.

In the same study, the patients reported that they had become aware of their body's reactions to different types of food. Before the dietary changes, the pain was considered intense and disabling, but after the dietary changes, there was a reduction or absence of pain, which had an impact on reducing the use of painkillers. Discomfort in the gastrointestinal tract decreased significantly and the abdomen became less swollen. There was also a reduction in colds, headaches, nausea and fever, as well as allergic and skin reactions.

The *online* exploratory study conducted by Krabbenborg *et al. (*2021) assessed women's quality of life and behavior through a food questionnaire, which was used to assess dietary characteristics, physical complaints and the mental state of the participants. The questionnaires were completed by 157 participants diagnosed with endometriosis by ultrasound, MRI or surgery between 2017 and 2019. The use of supplements and diets were assessed, as well as specific dietary adjustments, defined as limiting or adding

food consumption. Participants were advised to follow a type of dietary intervention and reduce dairy, gluten and soy and add vegetables as effective methods to decrease symptoms. In addition, the participants also used dietary supplements of vitamin D, B12, magnesium and omega 3.

Of the women who adhered to the diet, 46.6% mentioned that they followed it to reduce the symptoms of endometriosis. The diet is based on the consumption of fruit, nuts and fish, as well as crucial elements rich in anti-inflammatory or anti-estrogenic compounds, such as omega-3 fatty acids and antioxidants found in fruit, vegetables and oily fish, like the Mediterranean diet. We therefore hypothesized that a higher intake of these components could in fact reduce the pain associated with endometriosis, improving quality of life. As a result, half of the interviewees (55.5%) indicated that diet influenced endometriosis symptoms. The majority, 70% of the participants, reported that the diet decreased their symptoms, while 30% of them reported an increase in symptoms. Quality of life, however, was no different between the women who adjusted their diet and the women who did not.

Among the two studies mentioned, a relevant point to consider is the foods that are not in the Mediterranean diet and are related to the progression of the disease, such as red meat. A study conducted by Yamamoto *et al.* (2018) showed that the consumption of red meat contributed to an increase in pain symptoms in patients, due to its ability to increase concentrations of steroid hormones and provoke inflammatory reactions.

The results presented in the studies by Karlsson, Patel and Premberg (2020) and Krabbenborg *et al. (*2021) showed an improvement in symptoms with the removal of gluten, dairy products and soy, which, despite not being banned in the Mediterranean diet, showed significant results in reducing pelvic pain in the participants. Reducing gluten consumption can be beneficial in combating abdominal pain related to the gastrointestinal tract, constipation and abdominal distension, symptoms that are frequent among women with endometriosis. About milk, there are divergent studies on its side effects and benefits in relation to endometriosis. According to Nodler *et al.* (2020) there was a reduction in the rates of endometriosis diagnosis confirmed by laparoscopy during adulthood among those who consumed greater quantities of dairy products during adolescence. *(*2020), vitamin D and calcium present in dairy products have a potential positive biochemical and physiological impact on the risk of endometriosis.

However, there are some limitations to these studies that should be considered. There are few studies that focus directly on the Mediterranean diet and endometriosis, most of which are related to the effects of different dietary patterns, without delving into the interaction of the nutrients present in the Mediterranean diet. In addition, biochemical and symptom analysis studies would be necessary to corroborate the scientific results on the anti-inflammatory effect of this diet on endometriosis and on the pain reported by women. Thus, despite these limitations, there is evidence of benefits related to the consumption of the Mediterranean

diet in endometriosis, and it should be considered as a possibility of dietary interventions for the treatment of the disease, impacting on the reduction of symptoms and quality of life of these women.

CONCLUSIONS

Recent findings on the role of the Mediterranean diet seem promising as a strategy for reducing symptoms associated with endometriosis, causing pain relief and potential molecular biomarkers that act on endometrial functions, especially improving fetal development with proper embryo implantation and potentially improving fertility. The results also showed satisfactory adherence rates on the part of the women by including vegetables, fruit, whole grains, fish and poultry, as well as smaller portions of dairy products and a reduction in red meat, making it a viable treatment strategy. These strategies contribute to the quality of life and long-term health of young women with endometriosis, since they are considered functional foods, which can help modulate the pathological processes, inflammation and oxidative stress responsible for the chronic pain of the disease. Despite this, there are still a limited number of studies, requiring more evidence to support the indication of the Mediterranean pattern as an effective strategy in the treatment of endometriosis.

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