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Diet – A New Approach To Treating Endometriosis – What Is The Evidence?

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I. INTRODUCTION

Endometriosis affects over 70 million women worldwide and is more common than breast cancer and diabetes. A survey in 2005 showed that in the European Union, endometriosis cost member states more than €30bn a year in lost working days, and of the 7025 women with endometriosis who completed the survey, 82% reported that the condition had caused them to take time off work in the past five years. Endometriosis is a gynecological disorder characterized by the presence and growth of endometrial tissue outside the uterine cavity[1]. The prevalence of endometriosis among asymptomatic women ranges from 2–22%, while in women with infertility the incidence of endometriosis is 35% to 50%[2]. This pathology represents one of the most frequent gynecological disorders during women's reproductive age. Endometriosis is a hormone-dependent, chronic inflammatory gynaecological condition that causes pelvic pain symptoms impacting on the physical, mental and social wellbeing of reproductive-age women (Bianconi et al., 2007)[3]. Despite the high prevalence, which has been estimated to be between 6–10% (Parazzini et al., 1994)[4] and the recognized economic burden associated with the disease (Simoens et al., 2012)[5], its aetiology remains elusive. Various pathogenetic factors – menstrual, genetic, environmental, lifestyle – have been claimed to be implicated in the disease establishment and development (Viganò et al., 2004[6] and Viganò et al., 2012[7]).

The precise pathogenesis of endometriosis is unclear, and several theories have been proposed. Retrograde menstruation is widely accepted as a contributing factor to the disease but, as the phenomenon occurs in up to 90% of women, other factors in the pathogenesis of the disease have been suggested[8]. The immune response to endometriotic tissue outside the uterus seems to be impaired with inadequate removal of lesions as a result.

Increased exposure to oestrogens is a common link among several known risk factors for endometriosis. Local oestrogen production coupled with circulating oestrogen stimulates the proliferation of ectopic endometrial tissue potentially leading to endometriosis[9]. Menarche at early age, shorter menstrual cycle length, nulliparity and greater height are all risk factors for endometriosis that are also associated with increased levels of circulating oestrogen concentrations[10].

The risk of endometriosis is increased up to five times in siblings indicating that a genetic component is involved[11] . An autoimmune aetiology has also been implied[12] and , and exposure to environmental toxins has been suggested although results are not consistent[13] .

Dietary factors have been the focus of a growing number of endometriosis patient-directed books and web-sites. Unfortunately, there is little direct scientific evidence to support these suggestions. Diet may have a role in the aetiology of endometriosis through its influence on steroid hormone levels, among other potential mechanisms. Some observational studies have shown that plant-based diets and diets high in fibre increase oestrogen excretion and decrease concentrations of bioavailable oestrogen, and thus may lower endometriosis risk. Additionally, high-fat diets have been associated with increased serum oestrone, oestrone sulphate and oestradiol levels in premenopausal women, suggesting that diets low in fat and high in fibre may modify endometriosis risk by altering steroid hormone metabolism.

The role of nutrition in determining the establishment and progression of endometriosis has recently become a topic of interest, mostly due to the observation that some of the physiological and pathological processes associated with the disease, such as inflammation, oestrogen activity, menstrual cyclicity, organochlorine burden and prostaglandin metabolism, can be influenced by diet (Missmer et al., 2010)[14]. scientific research has demonstrated that diet and fat excess may strongly affect the incidence. Antioxidant properties of nutritional supplementation are associated with a significant reduction in inflammatory endometriosis-related markers, and with a suppressive effect on the endometrial-cell survival in vitro[15]. Two studies have found a positive association between oxidative stress and endometriosis. Reactive oxygen species may affect the growth of endometrial tissue. The presence of endometriosis increased oxidative stress and depletion of antioxidants may

contribute to excessive growth of endometrial cells. Significantly, lower levels of vitamin E were found in the peritoneal fluid than in plasma, suggesting that the peritoneal cavity has less antioxidant protection than serum, so the fluid containing the endometriosis might be more susceptible to oxidative stress. Antioxidant nutrients such as the vitamins A, C and E may be supportive.

Increased oxidative stress, a result of increased production of free radicals or depletion of the body's endogenous antioxidant defense, has been implicated in its pathogenesis. Oxidative stress is thought to promote angiogenesis and the growth and proliferation of endometriotic implants. Oxidative stress in the reproductive tract microenvironment is known to negatively affect sperm count and quality and may also arrest fertilized egg division leading to embryo death[16].

Considering the high prevalence of the disease and its difficult diagnosis and therapeutic management as a result of its complex pathogenesis, which is yet to be fully clarified, a question has been raised regarding whether women affected by endometriosis have certain nutritional peculiarities . The objectives of this review were to assess a possible association between dietary components and endometriosis from the existing literature and, if possible, to identify potential modifiable risk factors of the disease and to specify dietary recommendations for women suffering with this enigmatic gynecologic disorder.

II. Aims And Methods

A search for relevant studies was conducted. The databases used for researches were: CINAHL, Medline plus, Science Direct, SCOPUS,& PubMed. The following search terms were used: endometriosis and related factors like diet, fat, dairy products, fish, coffee and antioxidants .The inclusion criteria required the articles to be written in English &the studies on human beings only. The dates for the search were 2003-2013.

A total of 255 articles were identified by electronic searches , 110 articles were excluded for citation duplication and 92 were excluded based on abstracts and titles. 20 of which were full text articles focusing on endometriosis and diet. We excluded 8 articles , as 4 were based on serum levels of nutrients, 2 were animal studies and the other 2 were review articles. With detailed inspection and evaluation of the articles, 12 articles met the inclusion criteria.

A synthesis table was developed describing the characteristics of the studies used in the figure 1. The data extracted for the synthesis of the table included author, country, year, participants, methods, instruments study purpose and main findings.

III. Analysis Of Findings

Two authors reviewed the papers and independently selected the articles eligible for the review. If multiple published reports from a same study were available, we included only one with the most detailed information, or published more recently. Data were extracted by 2 investigators and discrepancies were resolved by discussion.

3.1 Results

A total of 12 studies conducted in 6 countries like USA-5, Italy-3, Japan-1, Mexico-1, Belgium-1, and Brazil-1 met the inclusion criteria for this review. The articles were published between the years 2003-2012. Details of all these quantitative studies are shown in Table.1. Majority of the studies were case control studies -4,one cohort study, 3 retrospective studies, 1 randomized experimental study, comparative studies-2, single blinded clinical study. Majority of the studies used FFQ (Food frequency questionnaire) to assess the dietary intake. Clinical trials used lab values of anti-oxidant markers additionally to assess their dietary patterns.

Holly R. Harris et al.,(2013)[17] investigated whether intake of dairy foods, nutrients concentrated in dairy foods, and predicted plasma 25-hydroxyvitamin D (25(OH)D) levels were associated with incident laparoscopically confirmed endometriosis among 1,385 cases. Intakes of total and low-fat dairy foods were associated with a lower risk of endometriosis. Women consuming more than 3 servings of total dairy foods per day were 18% less likely to be diagnosed with endometriosis than those reporting 2 servings per day (rate ratio = 0.82, 95% confidence interval: 0.71, 0.95; P trend = 0.03). In addition, predicted plasma 25(OH)D level was inversely associated with endometriosis. Women in the highest quintile of predicted vitamin D level had a 24% lower risk of endometriosis than women in the lowest quintile (rate ratio = 0.76, 95% confidence interval: 0.60, 0.97; P trend = 0.004). Findings suggested that greater predicted plasma 25(OH)D levels and higher intake of dairy foods are associated with a decreased risk of endometriosis.

Marziali et al.,(2012)[18], conducted a retrospective study to evaluate the effectiveness of gluten-free diet for 12 months on endometriosis-related pain and quality of life in patients with endometriosis-related chronic pelvic pain. Two hundred and seven patients with severe painful endometriosis-related symptoms entered the study. At enrolment time, the baseline values of painful symptoms were assessed by Visual Analogue Scale (VAS) for dysmenorrhoea, non-menstrual pelvic pain, and dyspareunia. A gluten-free diet was submitted to all patients and a new evaluation was performed after 12 months of diet. Student t test was used for statistical analysis. At 12 month follow-up, 156 patients (75%) reported statistically significant change in painful symptoms

(P<0.005), 51 patients (25%) reported not improvement of symptoms. No patients reported worsening of pain. A considerable increase of scores for all domains of physical functioning, general health perception, vitality, social functioning, and mental health was observed in all patients (P<0.005).

Ana Luiza Savaris and Vivian F. do Amaral, (2011)[19],conducted a study to assess the Nutrient intake, anthropometric data and correlations with the systemic antioxidant capacity of women with pelvic endometriosis. Twenty-five women with endometriosis and twenty controls were selected and evaluated to determine calorie and nutrient intake, to obtain data on body composition and analyze antioxidant capacity by measuring total serum thiol levels using DTNB (5,5′-dithiobis-(2-nitrobenzoic acid). Mean total daily calorie intake in the women in the endometriosis group was significantly higher than that of the women in the control group ($p = 0.005$). With respect to nutrient intake, the only statistically significant difference found referred to a higher intake of fiber in the endometriosis group and of polyunsaturated fatty acids in the control group ($p < 0.05$). They also found that women with endometriosis were characterized by a greater prevalence of overweight, presented with a high intake of calories and fiber, had lower intake of polyunsaturated fatty acids and had reduction in systemic antioxidant capacity. There was no correlation of antioxidant capacity with nutrient intake or overweight.

Britton Traberta et al.,(2010)[20], evaluated dietary risk factors for endometriosis in a population-based case–control study. Cases were 284 Group Health (GH) enrollees aged 18–49 years with newly diagnosed, surgically confirmed endometriosis. Controls were 660 randomly selected age-matched female GH enrollees without a history of endometriosis. Nutrients and selected food groups were assessed using the Women's Health Initiative FFQ. OR(odds ratio) of endometriosis risk associated with dietary exposures were estimated using unconditional logistic regression and adjusted for identified covariates. Increased total fat consumption was associated with decreased endometriosis risk (fourth quartile v. lowest: OR 0•5, 95 % CI 0•2, 1•0, P-trend = 0•12). Increased β-carotene consumption and servings/d of fruit were associated with increased risk (β-carotene third quartile v. lowest: OR 1•7, 95 % CI 1•1, 2•6; fourth quartile v. lowest: OR 1•6, 95 % CI 1•0, 2•5, P-trend 0•16; fruit >2 servings/d v. < 1: OR 1•5, 95 % CI 1•0, 2•3, P-trend = 0•04). They also found a suggestion of decreased endometriosis risk associated with the consumption of dairy products (2 servings/d v. ≤ 1: OR 0•6, >2 servings/d v. ≤ 1: OR 0•7), but this association was not statistically significant for the highest tertile.

Stacey A. Missmer et al.,(2010)[21], investigated the relation between dietary fat intake and the risk of endometriosis in a retrospective study, among 1199 cases of laparoscopically confirmed endometriosis. They used Cox proportional hazards models adjusted for total energy intake, parity, race and body mass index at age 18, and assessed cumulatively averaged fat intake across the three diet questionnaires. Although total fat consumption was not associated with endometriosis risk, those women in the highest fifth of long-chain omega-3 fatty acid consumption were 22% less likely to be diagnosed with endometriosis compared with those with the lowest fifth of intake [95% confidence interval (CI) = 0.62–0.99; P-value, test for linear trend (Pt) = 0.03]. In addition, those in the highest quintile of trans-unsaturated fat intake were 48% more likely to be diagnosed with endometriosis (95% CI = 1.17–1.88; Pt = 0.001).

In the study by Jennifer Mier-Cabrera et al.,(2009)[22], antioxidant intake among women with and without endometriosis were compared. Women with (WEN, n = 83) and without endometriosis (WWE, n = 80) were interviewed using a Food Frequency Questionnaire to compare their antioxidant intake (of vitamins and minerals). Then, the WEN participated in the application of a control (n = 35) and high antioxidant diet (n = 37) for four months. The high antioxidant diet (HAD) guaranteed the intake of 150% of the suggested daily intake of vitamin A (1050 µg retinol equivalents), 660% of the recommended daily intake (RDI) of vitamin C (500 mg) and 133% of the RDI of vitamin E (20 mg). Oxidative stress and antioxidant markers (vitamins and antioxidant enzymatic activity) were determined in plasma every month. Comparison of antioxidant intake between WWE and WEN showed a lower intake of vitamins A, C, E, zinc, and copper by WEN ($p < 0.05$, Mann Whitney Rank test). The selenium intake was not statistically different between groups. During the study, the comparison of the 24-hour recalls between groups showed a higher intake of the three vitamins in the HAD group. An increase in the vitamin concentrations (serum retinol, alpha-tocopherol, leukocyte and plasma ascorbate) and antioxidant enzyme activity (superoxide dismutase and glutathione peroxidase) as well as a decrease in oxidative stress markers (malondialdehyde and lipid hydroperoxides) were observed in the HAD group after two months of intervention. These phenomena were not observed in the control group.

Sesti et al., (2009)[23] performed a randomized comparative trial to investigate the rate of recurrence of endometriosis following laparoscopic surgery. Postoperatively, the women were divided into four groups who received different treatments for 6 months: no treatment (placebo), gonadotrophin-releasing hormone analogue (GnRH-a), oral contraception or nutritional supplements including fish oils. After 18 months, transvaginal ultrasonographic follow-up after surgery there was no significant difference in the recurrence rate between the three treatment groups and the placebo group. Second-look laparoscopy was performed on a clinical basis and confirmed the ultrasonographic suspicion of recurrence of endometrioma in all cases. A 6-month course of hormonal suppression treatment or dietary therapy after laparoscopic cystectomy had no significant effect on the recurrence rate of ovarian endometriosis when compared with surgery plus placebo.

Masaki Tsuchiya.,(2007)[24], examined associations among soy isoflavone intake, estrogen receptor 2 (ESR2) gene polymorphisms and risk of endometriosis among women of age 20–45 years old. A total of 138 eligible women were diagnosed laparoscopically and classified into 3 subgroups: control (no endometriosis), early endometriosis (stage I–II) and advanced endometriosis (stage III–IV). Urinary levels of genistein and daidzein were measured as markers for dietary intake of soy isoflavones, and genotyped ESR2 gene RsaI polymorphisms. Higher levels of urinary genistein and daidzein were associated with decreased risk of advanced endometriosis (P for trend 0.01 and 0.06, respectively) but not early endometriosis. For advanced endometriosis, the adjusted odds ratio for the highest quartile group was 0.21 (95% confidence interval 0.06–0.76) for genistein and 0.29 (0.08 –1.03) for daidzein, when compared with the lowest group. Inverse associations were also noted between urinary isoflavones and the severity of endometriosis (P for trend 0.01 for genistein and 0.07 for daidzein).

Jean Francois Heilier et al.,(2006)[25], compared risk factors associated with both forms of the endometriosis, with a particular attention to potential sources of organochlorine exposure. This matched case–control study with prospective recruitment included 88 triads (PE–DEN–control). All women were face-to-face interviewed with FFQ, and serum dioxin and polychlorinated biphenyl measurements were available for 58 of them. Alcohol consumption (odds ratio (OR): 5.82 [confidence interval at 95% (95%CI) 1.20–28.3]) in DEN and low physical activity at work for DEN (OR: 4.58 [95%CI 1.80–11.62]) and PE (OR: 5.61 [95%CI 1.90–16.60]) were traced as significant risk factors. Organochlorine-related factors (use of tampons, occupational or environmental exposure) were not related to the disease. The current consumption of foodstuffs that were more likely to contribute to organochlorine body burden did not differ among the groups. Only some of these fatty foodstuffs (marine fish, pig meat) were traced by multiple regression analysis as significant determinants of organochlorine body burden, explaining only a small fraction (20%) of the interindividual variation of organochlorine body burden.

Within a study investigating persistent organic compounds and endometriosis, L.W. Jackson et al., (2005)[26] evaluated the association between oxidative stress and endometriosis. Women aged 18–40 years who were undergoing laparoscopy were contacted to participate in the study (n=100); 84 were eligible and agreed to be interviewed; 78 provided blood specimens. Four markers of oxidative stress and antioxidant status were measured in serum for 61 women(i) thiobarbituric acid-reacting substances (TBARS), which measure primarily malondialdehyde derived from lipid peroxidation, as well as other breakdown products from oxidatively modified proteins, carbohydrates and nucleic acids (Guichardant et al., 2004); (ii) 8-F2-isoprostane for a stable end-product of oxidized lipids derived from arachidonic acid (Fam and Morrow, 2003); (iii) fat-soluble antioxidants (vitamin A, vitamin E, β-carotene and lycopene) reflecting micronutrient antioxidant protection in serum; and (iv) paraoxonase (PON1) activity. Thirty-two women had visually confirmed endometriosis at laparoscopy while 52 did not, including 22 undergoing tubal ligation and 30 with idiopathic infertility. There was a weak association between thiobarbituric acid-reactive substances (nmol/ml) and endometriosis, after adjusting for age, body mass index, current smoking, hormone use in the past 12 months, gravidity, serum vitamin E, serum estradiol, and total serum lipids (β=1.18; 95% CI–0.04, 2.39). These results suggested that oxidative stress might play a role in the development and progression of endometriosis.

Stacey A. Missmer et al.,(2004)[27] investigated the relations of demographic, anthropometric, and lifestyle factors with endometriosis in 1,721 cases of laparoscopically confirmed endometriosis were reported among women with no past infertility. The authors observed no association with, caffeine intake and endometriosis.

Parazzini et al.,(2003)[28], analysed data collected in the framework of two case–control studies to offer data on the relationship between diet and risk of pelvic endometriosis. Cases were 504 women aged <65 years (median age 33 years, range 20–65) with a laparoscopically confirmed diagnosis of endometriosis. Controls were 504 women (median age 34 years, range 20–61) admitted for acute non-gynaecological, non-hormonal, non-neoplastic conditions. Compared to women in the lowest tertile of intake, a significant reduction in risk emerged for higher intake of green vegetables [odds ratio (OR)=0.3 for the highest tertile of intake] and fresh fruit (OR=0.6), whereas an increase in risk was associated with high intake of beef and other red meat (OR=2.0) and ham (OR=1.8). Consumption of milk, liver, carrots, cheese, fish and whole-grain foods, as well as coffee and alcohol consumption, were not significantly related to endometriosis which suggested a link between diet and risk of endometriosis.

IV. Discussion

The literature related to endometriosis and diet is very little and inconsistent. In this review we comprehensively evaluated the impact of diet in the emergence and progression of endometriosis.

4.1 Endometriosis and Fat intake

Stacey A. Missmer et al.,(2010)[21], suggested that intake of trans-unsaturated fats was associated with a higher risk of endometriosis . Intakes of saturated fat and monounsaturated fat, were not associated with endometriosis risk. Interestingly, palmitic acid intake, a saturated fat was significantly related to increased

endometriosis risk . In contrast to the above findings, Britton Traberta et al.,(2010)[20], reported an inverse associations with endometriosis risk for saturated-, monounsaturated- and trans-fat intake. The inadequate polyunsaturated fatty acids (PUFAs) intake by the women with endometriosis favors inflammation and consequently oxidative stress. Ana Luiza Savaris and Vivian F. do Amaral, (2011)[19].

In the Italian case–control study, no association emerged between oil intake and risk of endometriosis whereas an increase in risk for endometriosis was associated with high intake of beef and red meat and ham Parazzini et al.,(2003)[28]. Jean Francois Heilier et al.,(2006)[25], reported the consumption of marine fish and pig meat as significant determinants of peritoneal endometriosis and deep endometriotic nodules.

However, intake of long-chain omega-3 fatty acids was associated with a lower risk of endometriosis Stacey A. Missmer et al.,(2010)[21]. Although a trend for a decreased risk could be observed in Parazzini et al.,(2003)[28] while a complete absence of any association was found by Britton Traberta et al.,(2010)[20]. In addition a dietary therapy with Omega 3 and Omega 6 fatty acids yielded no significant effect on the recurrence rate of endometriosis Sesti et al., (2009)[23] .

4.2 Endometriosis and Calcium

The largest study by Holly R. Harris et al.,(2013)[17] reported a significantly lower rate of endometriosis among women with greater predicted plasma 25(OH)D levels and among women with a higher intake of dairy foods. Calcium, vitamin D, and magnesium intakes from foods (including fortified foods) were also inversely related to endometriosis. In addition Britton Traberta et al.,(2010)[20] also found a decreased endometriosis risk associated with consumption of dairy products but this association was not statistically significant for the highest tertile and suggested that specific dietary components may be associated with endometriosis risk. In addition Parazzini et al.,(2003)[28] also suggested milk consumption was not significantly related to endometriosis.

4.3 Endometriosis and fiber

The consumption of carrot and whole grain foods were not significantly related to endometriosis Parazzini et al.,(2003)[28]. The inadequate fiber intake by the women with endometriosis favors inflammation and consequently oxidative stress. Ana Luiza Savaris and Vivian F. do Amaral, (2011)[19].

4.3 Endometriosis and antioxidant diet

Many studies have focused on the importance of antioxidant diet in abolishing oxidative stress markers and improve antioxidant markers in women with endometriosis.

Jennifer Mier-Cabrera et al.,(2009)[22], reported the application of the high antioxidant diet in women with endometriosis increased the peripheral antioxidant enzymatic activity & decreased the peripheral concentration of oxidative stress markers . No positive association was found between antioxidant nutrient intake and a reduction in systemic antioxidant capacity Ana Luiza Savaris and Vivian F. do Amaral, (2011)[19].

L.W. Jackson et al., (2005)[26] indicated that the markers of oxidative stress and antioxidant status vitamin A, lycopene, β carotene and vitamin E were not found to be associated with endometriosis. Masaki Tsuchiya.,(2007)[24], found that higher urinary levels of isoflavones was associated with a reduced risk of advanced endometriosis , but not early endometriosis.

Sesti et al., (2009)[23] reported that the dietary therapy with vitamins B6 , A,C,E and minerals salts like Ca, Ma, Se, Zn, Fe, yielded no significant effect on the recurrence rate of endometriosis . In addition Britton Traberta et al.,(2010)[20], found Increased β-carotene consumption was associated with increased endometriosis risk. Whereas other macronutrients and micronutrients were not significantly associated with endometriosis risk.

4.4 Endometriosis and caffeine

Stacey A. Missmer et al.,(2004)[27] did not observe any association of endometriosis with the amount and frequency of caffeine consumed per day .

The current evidences from our review allow us to conclude that dietary factors play an important role in prevention and progression of endometriosis and is imperative as a treatment modality in improving the quality of life of women suffering from endometriosis.

V. Implications For Practice

Based on the results shown in the present manuscript, we can suggest that health education in regard to the dietary management in endometriosis is the need of the hour in improving the quality of life of women with endometriosis. The Nurses and other health professionals in primary care plays an essential role in health promotion through disease management and infertility prevention by providing support and much needed information to the patient with endometriosis. They can also facilitate quality of care and manage treatments effectively to improve quality of life, reduce pain, and prevent further progression of disease. Practice

recommendations include timely diagnosis, pain management, infertility counseling, patient education including dietary factors, and support for quality of life issues.

Awareness through mass media in the schools, colleges and other public places on the aspects of dietary risk factors in endometriosis can be made available by the health care authorities. Continuing nursing education programs on endometriosis and diet are mandatory to improve evidence-based practice.

More research is needed on dietary factors and endometriosis in other parts of the world, as only studies in western European countries are presently available. And also studies on low fat vegetarian diet and endometriosis also can be done in future for evidence.

VI. Conclusion

There is an urgent need to improve understanding of the impact of dietary components on the risk of endometriosis in order to modify and/or prevent this prevalent gynecological disease. Overall, the literature suggested that increased consumption of Anti-oxidant diets, omega-3 FAs, fish oils and PUFAs has a positive effect on endometriosis, indicating that there may be modifiable risk factors. The results of the study suggests that higher intake of green vegetables and fresh fruit can lower the risk of endometriosis. Further analyses will help to utilize dietary modification as a treatment modality which underlie as a risk factor in this prevalent, poorly understood disease.

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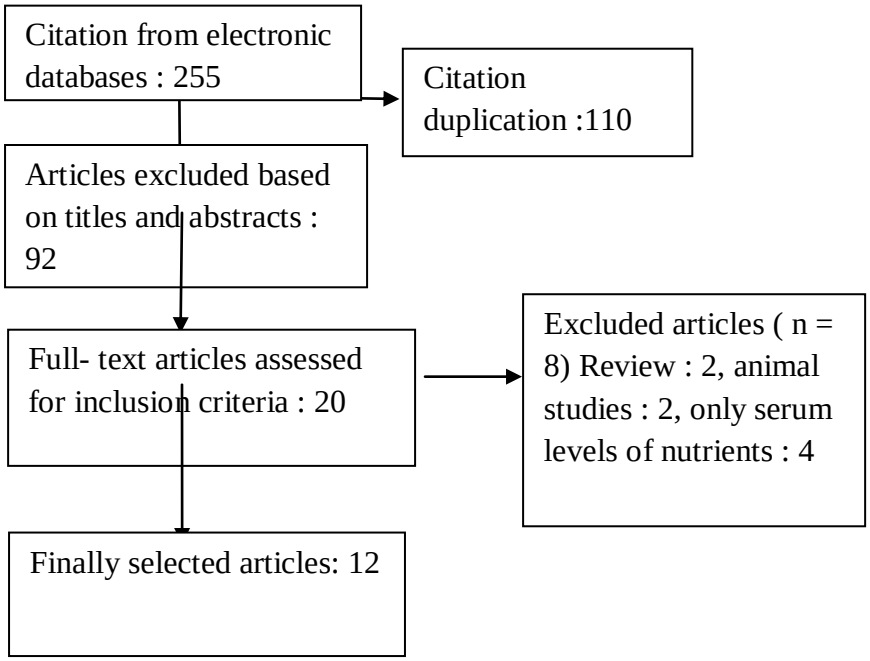

Figure:1. Flow chart showing methodological pathway

Figure:2. Dietary factors in prevention of Endometriosis

Table.1-Summary of the articles with author, country, year, participants, methods, instruments, study purpose and main findings

SL. NO	Author, Country and Year	Participants	Methods	Instrument	Study purpose	Main findings
1.	Holly R. Harris et al., (2013) USA	1,385 cases (25-42 years)	prospective cohort study	food frequency questionnaire (FFQ)	whether intake of dairy foods, nutrients concentrated in dairy foods (calcium, vitamin D, magnesium, and phosphorus), and predicted plasma 25(OH)D levels were associated with incident laparoscopically confirmed endometriosis	Intakes of total and low-fat dairy foods were associated with a lower risk of endometriosis. Findings suggest that greater predicted plasma 25(OH)D levels and higher intake of dairy foods are associated with a decreased risk of endometriosis
2.	Marziali M et al.,(2012). ITALY	207 patients.	Retrospective study	A gluten-free diet was submitted to all patients and a new evaluation was performed after 12 months of diet with VAS &SF-36 scales.	To evaluate the effectiveness for the outcomes of endometriosis-related pain and quality of life of gluten-free diet in a follow-up of 12 months.	At 12 month follow-up, 156 patients (75%) reported statistically significant change in painful symptoms, 51 patients (25%) reported not improvement of symptoms. No patients reported worsening of pain. A considerable increase of scores for all domains of physical functioning, general health perception, vitality, social functioning, and mental health was observed in all patients.
3.	Britton Traberta et al., (2011) USA	944 Women (18-49 years)	Population-based case-controlled study	Self-administered women's health initiative FFQ	The purpose of this analysis was to further investigate the role of diet – as a risk factor for endometriosis.	Increased total fat consumption was associated with decreased endometriosis risk. Increased β-carotene consumption and servings/d of fruit were associated with increased risk.
4.	Ana Luiza Savaris, and Vivian F. do Amaral,(2011), Brazil	25 women with endometriosis and 20 controls (18-35 years)	Comparative Study	24 Hours recall and measuring Thiol levels for Anti-oxidant capacity.	whether women affected by endometriosis have certain nutritional peculiarities associated with nutrient intake	Mean total daily calorie intake in the women in the endometriosis group was significantly higher than that of the women in the control group. With respect to nutrient intake, the only statistically significant difference found referred to a higher intake of fiber in the endometriosis group and of polyunsaturated fatty acids in the control group.
5.	Stacey A. Missmer et al., (2010), USA	1199 cases (25-42 years)	Retrospective study	Dietary fat was assessed via food frequency questionnaire and Cox proportional hazards models	To investigate the relation between dietary fat intake and the risk of endometriosis	women in the highest fifth of long-chain omega-3 fatty acid consumption were 22% less likely to be diagnosed with endometriosis. Those in the highest quintile of trans-unsaturated fat intake were 48% more likely to be diagnosed with endometriosis
6.	Jennifer Mier-Cabrera et al., (2009)-Mexico	Women (30-40 years) 83/80	Randomized Experimental Study	Food Frequency Questionnaire (FFQ), a multiple-step 24-hour recall	To compare the antioxidant intake among women with and without endometriosis	Comparison of antioxidant intake between WWE and WEN showed a lower intake of vitamins A, C, E, zinc, and copper by WEN
7.	Francesco Sesti, et al., (2009), Italy	259 women.	Randomized comparative trial	clinical gynecologic examination, and transvaginal ultrasonography	To assess the recurrence rate of endometriosis after laparoscopic cystectomy plus hormonal suppression treatment or plus dietary therapy compared to post-operative placebo.	A 6-month course of hormonal suppression treatment or dietary therapy after laparoscopic cystectomy had no significant effect on the recurrence rate of ovarian endometriosis when compared with surgery plus placebo.
8.	Tsuchiya M et al., (2007). Japan	138 eligible women in 3 subgroups (20-45 years)	Case control study	Measured urinary levels of genistein and daidzein as markers for dietary intake of soy isoflavones.	Examined associations among soy isoflavone intake, and risk of endometriosis.	Higher levels of urinary genistein and daidzein were associated with decreased risk of advanced endometriosis but not early endometriosis.
9.	Jean-Franc-ois Heilier et al. (2006). Belgium	264 women (21-50 years)	Matched case–control study	FFQ, Serum dioxin and polychlorinated biphenyl measurements	To compare risk factors associated with both forms of the disease, with a particular attention to potential sources of organochlorine exposure.	Only some of these fatty foodstuffs (marine fish, pig meat) were traced as significant determinants of organochlorine body burden, explaining only a small fraction (20%) of the inter individual variation of organo chlorine body burden.
10.	L.W. Jackson E.F. et al., (2005), USA	32 women (18-40 years)	Single-blinded clinical study	Limited diet information and Four markers of oxidative stress and antioxidant status were measured.	To evaluate the association between oxidative stress and endometriosis.	There was a weak association between thio barbituric acid-reactive substances and endometriosis.
11.	Stacey A. Missmer et al.,(2004), USA	1,721 cases (25-29 years)	Retrospective study	Current intake of caffeine (derived from reported consumption of caffeinated beverages)	Investigated the relations of demographic, anthropometric, and lifestyle factors with endometriosis. were reported among women with no past infertility.	The authors observed no association with, caffeine intake and endometriosis.
12.	Parazzini et al. (2003), Italy	504 Women (Age 20–65 years)	Hospital-based case control study	Weekly consumption of selected dietary items(Validated FFQ)	To find the relationship between the diet and pelvic Endometriosis.	A reduction in risk for high intake of green vegetable and fruit and an increased risk for intake of ham, beef and other red meat.