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Current dietary approaches in ulcerative colitis: Exploring implications for women's health

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Abstract

Ulcerative colitis (UC) affects many individuals, significantly impacting their quality of life (QoL) and leading to severe medical complications. Unfortunately, the adverse health outcomes of UC are often overlooked, particularly in relation to women's health, including pregnancy, lactation, sexuality, and menopause. The main objective of this review is to provide guidance for women with UC, helping them navigate their disease and gain knowledge about the effects of nutrition on their overall well-being. A literature search was conducted between October 1, 2022, and July 14, 2023, using books, documents, and journal articles. Internet-based sites such as PubMed, ScienceDirect, EBSCO, and Google Scholar were also utilized. It became evident that women with UC are greatly affected during active periods of the disease, which can significantly reduce their QoL. Pregnancy, sexuality, menstruation, and puberty were among the factors most negatively impacted by the disease. A diet rich in anti-inflammatory foods, probiotics, berberine, turmeric, and vitamin D was found to have a positive association with UC. However, the consumption of a Western dietary pattern or a meat-based diet increases the risk of the disease. In conclusion, maintaining remission and following dietary patterns that suppress inflammation may help reduce complications and improve QoL in women. Our data suggest that all women diagnosed with UC should be well-informed and educated about the disease and its consequences. Further studies are needed to investigate the relationship between ongoing dietary habits and the treatment of UC in women. Our data suggest that all women diagnosed with UC should be well-informed and educated about the disease and its consequences. Further studies are needed to investigate the relationship between ongoing dietary habits and the treatment of UC in women.

Keywords: ulcerative colitis, dietary modifications, women's health, disease management

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Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) that can affect many young individuals and is classified as an uncontrollable disease by the Japanese Ministry of Health, Labor, and Welfare [1,2]. It is the most widespread type of IBD and is relatively common among chronic intestinal diseases [3]. Over time, the incidence and prevalence rates of UC have been increasing. Canada, Northern Europe, and Australia have the highest reports of new cases, specifically 0-19.2 per 100,000 in North America. Similarly, the reported prevalence rates are highest in Canada and Europe [4]. Increased urbanization rates expose individuals to environmental pollutants and lifestyle changes. Another factor may be the increasing rate of Westernization in many cultures, which mainly includes changes in eating patterns that can alter the host's microbiome and adaptive immunity [5]. The colon is the most affected area in UC, and there is often a strong family history of IBD in patients with at least one affected first-degree relative [4]. The majority of genetic information related to UC comes from genome-wide association studies (GWAS) in IBD, which have identified multiple genetic polymorphisms that contribute to the disease. Out of the 200 loci correlated with IBD, 15% are specific to UC [5]. The first peak incidence of UC occurs among those aged 20-29, while a second smaller peak occurs in individuals aged 60-89, known as the seventh to ninth decades of life [4].

Factors associated with developing UC include a fatty diet, stress, medication use, quitting tobacco use, high socioeconomic status, and a Westernized lifestyle [6]. Although the exact cause of UC is unclear, it is known that the intestinal bacterial population can trigger an inappropriate and exaggerated immune response in individuals who are genetically susceptible, leading to damage in the intestinal tissue. In addition to the genetic factors in UC patients, it is important to note that UC involves dysregulation of the body's natural defense system against antigens, most commonly free-living bacteria [7]. The pathology of UC involves inflammation of the mucosa, starting in the rectum and extending to all or part of the large intestine [4]. UC is primarily characterized by bloody stool and diarrhea, but can also cause symptoms such as fatigue, incontinence, increased bowel movements, mucus release, nocturnal defecation, abdominal cramps, fever, weight loss, loss of appetite, and tenesmus [4]. Diagnosis of UC is confirmed based on clinical symptoms, findings on colonoscopy or sigmoidoscopy showing continuous colonic inflammation starting in the rectum. Therefore, the diagnosis is made through the pathological discovery of chronic colitis [6]. Approximately half of patients with severe UC require surgery within the first few years of their disease. The primary risks of surgery include hemorrhage, infection, sepsis, and neurological complications, and the preferred surgical option is ileal-pouch anal anastomosis [4].

Women's health is significantly affected during their reproductive years, with issues related to sexuality, fertility, pregnancy, delivery mode, lactation, menopause, menstruation, and puberty being of particular importance [8]. Although the general clinical course of UC in pregnant women is not significantly different from the general population, if the disease is active during pregnancy, there is a 60% chance that it will worsen [1]. A 2014 study of 121 women with IBD found that 25% experienced changes in their menstrual cycle intervals and 21% experienced changes in the duration of flow in the year before their diagnosis [9]. Poorly controlled IBD has also been associated with a delay in the onset of puberty [10]. Some women with UC choose not to have children due to concerns about the adverse effects of medications on the unborn child, complications during delivery and lactation, fertility issues, and pregnancy complications such as congenital abnormalities, preterm birth, small for gestational age (SGA) babies, and spontaneous abortion [1]. The rate of voluntary childlessness is estimated to be up to 17% in women with UC compared to 6% in the general population [8]. While most mothers are encouraged to breastfeed their babies for at least six months, women with IBD often discontinue breastfeeding due to concerns about medication [11].

Since patients with IBD have reduced absorption of nutrients in their intestines, they are more likely to have deficiencies in specific nutrients, especially during active stages of the disease. This can lead to severe malnutrition and negative outcomes in pregnancy, such as premature birth or babies with a small size for gestational age. In addition to the disease itself, the mother's nutritional status is also important because nutrients are mainly transferred to the fetus through the placenta [12]. The exact cause of increased disease activity during pregnancy in women with IBD is not fully understood, but a study has shown that markers of inflammation, particularly tumor necrosis factor-alpha (TNF-a) and interleukin-6 (IL-6), are elevated in intestinal tissues [13]. The diet plays a significant role in modifying the microbiome and the immune response in the intestines, making nutrition a crucial factor in the development of IBD. Adequate intake of dietary fibers, primarily from fruits and vegetables, omega-3 fatty acids, iron, and vitamin D, may help improve disease activity by preventing inflammation. Therefore, the focus should be on inducing and maintaining remission in the clinical management of UC and ensuring sufficient nutrient intake through diet [14].

This study aims to provide guidance for women with UC on managing their disease activity without compromising their quality of life. It also aims to educate these patients about current dietary approaches for UC, including which food groups to consume and which dietary patterns to follow in order to manage their disease. The ultimate goal is to empower women with UC to prevent disease activity and maintain remission, as this is the most important factor to consider. Another objective of this study is to encourage women to seek medical help and consult healthcare professionals before complications arise. Therefore, clinicians and health systems should provide specialized care and support for these patients.

Women's Health and UC

Women with UC are at a higher risk of adverse pregnancy outcomes, as shown by a nationwide study. The study found increased inflammation in endoscopic procedures and a higher risk of surgery related to IBD in women with histological inflammation. Nearly half of the patients in this group experienced an increased risk of premature birth and having babies with a small size for gestational age due to active disease. It is recommended that pregnant patients with IBD consult with a Maternal-fetal medicine specialist, especially if they have undergone surgery for IBD. The gastroenterologist should coordinate the care of women

with UC throughout their pregnancy, taking into account the severity of the disease and the pregnancy status. A clear and understandable treatment plan should be provided to manage the disease from conception to postpartum.

During the active period of the disease, when patients may struggle to gain weight, the involvement of a nutritionist may be necessary. A psychiatrist can provide support for anxiety and depression, which often increase during pregnancy and IBD. Additionally, a lactation specialist can assist these patients with their IBD medications [15].

There is no evidence that vaginal delivery influences the risk of IBD development in offspring. Women with IBD who have good control of inflammation during pregnancy are more likely to have a healthy pregnancy [15]. A meta-analysis showed no significant differences in the incidence of Caesarean section, therapeutic abortions, or ectopic pregnancies between women with active and inactive IBD. However, overall, women with IBD are more likely to deliver by Caesarean section than those without IBD [1].

Breastfeeding is the recommended primary source of nutrients for infants, and it is advised that almost all mothers breastfeed for at least six months. However, many women with IBD discontinue breastfeeding due to concerns about medication [11]. These mothers should be encouraged to continue breastfeeding, as disease flares may occur postpartum. A multidimensional approach, involving specialized physicians and dietitians, should be provided for high-risk pregnancies.

Puberty onset can be affected in girls with IBD, leading to delayed puberty and anovulatory fertility, primarily due to inadequate or excessive nutrition. Symptoms of IBD can also worsen during menstruation, including increased intestinal motility [16]. A study found that healthy controls experienced more frequent bowel movements during menstruation compared to IBD patients [17]. Late puberty onset has also been associated with other risk factors, including failure to grow, malnutrition, poor nutritional status, corticosteroid use, and persistent flares [10].

A cohort study showed that women with IBD experience early onset of menopause compared to non-affected women. Early and premature menopause is associated with numerous long-term negative health effects, including a higher risk of osteoporosis and heart disease. Therefore, early menopause can further increase the risks associated with IBD in women [18].

Sexual dysfunction can occur in patients with IBD, leading to emotional and behavioral issues. Problems with sexual activity not only affect social relationships but also reduce personal abilities and productivity. A study found that a higher number of patients with UC were in an active disease period, resulting in higher levels of anxiety and depression compared to those in remission [19]. A meta-analysis suggested that the use of oral contraceptives substantially increases the risk of developing UC and discontinuing their use reduces the risk. Therefore, women with IBD should be advised to discontinue oral contraceptives [20].

Role of Diet in UC Women's Health

Western dietary pattern

As mentioned, IBD has increased in most countries due to the adoption of a Western dietary pattern. This pattern includes high intakes of refined grains, unhealthy fats such as saturated fatty acids and trans-fat, and low intakes of dietary fiber and whole grains. A systematic review found that North and South America had a high intake of ultra-processed foods, which increased the risk of disease development. Additionally, these countries had the highest consumption of processed meat, soft beverages, refined sugars, and salty snacks. The association with increased disease risk can be explained by the substantial number of additives, preservatives, and sodium in this dietary pattern [21]. This dietary pattern triggers an inflammatory environment that can affect intestinal permeability and change the content of the gut microbiota [22].

The outcomes of a case-control study revealed that a Western dietary pattern was positively associated with the risk of breast cancer in both pre- and post-menopausal women. This may be due to the consumption of exogenous hormones through the ingestion of red/processed meat and poultry, which can activate the hormones in breast tissue and stimulate the proliferation and growth of tumors. Ingesting high glycemic index foods, such as cereals high in sugar, dairy high in fat and sugar, and sugary beverages, may also increase estrogen levels and promote the proliferation and growth of tumor cells [23].

Meat-based diet

A different study illustrated that a meat-based diet, including poultry, red meat, and processed meat, also known as a carnivorous diet, correlated with a higher risk of UC [24]. Proteins with high sulfur and cysteine content, which sulfate-reducing bacteria utilize to generate hydrogen sulfide (H2S), can exacerbate IBD flares since they have detrimental inflammatory effects [25]. In line with this study, a protein-rich diet, including beef, burger, canned tuna, chicken, chicken liver, and eggs, is associated with an increased risk of IBD [22].

Iron-rich diet

Iron absorption can be adversely impacted by inflammation in the gastrointestinal system, especially in conditions such as UC, which reduces iron absorption and causes iron deficiency in many women. As a result, the quality of life decreases, and hospitalization rates increase due to anemia in these patients. Therefore, UC patients are recommended to consume the required amount of iron from either iron-rich foods or supplements. Guidelines for patients at risk for iron deficiency include eating meat and fish, green vegetables (although compounds that inhibit iron absorption may be present), legumes (if tolerated by patients), reducing the consumption of caffeine as it inhibits the absorption of iron, and most importantly, eating foods that are rich in non-heme iron with vitamin C to enhance absorption. For example, spinach and lemon juice. Women with an iron deficiency should be aware of iron inhibitors such as phytates, phosphates, and calcium [26]. Processes like implantation, placenta growth, angiogenesis, and nutrient transfer to the fetus from the mother require essential amino acids. However, supplements containing them are costly and only profitable for some patients. A low-cost alternative is bone broth, which provides substantial amounts of minerals, vitamins, collagen, and essential amino acids of more than 50%. It has been reported that bone broth helped diminish the expression of inflammatory cytokines such as interleukin-1 beta (IL-1B), IL-6, and TNF-a [27,28].

Anti-inflammatory diet

A randomized, placebo-controlled trial found that an anti-inflammatory diet, including increased consumption of dietary fiber, probiotics, n-3 fatty acids, fruits, and vegetables (antioxidants), and decreased intake of red and processed meat and refined sugar, positively correlated with reduced disease risk. Not only did the composition of the gut microbiome change, but the fecal calprotectin level, which is a marker of inflammation in the colon and relapse of disease, was also lower. A substantial increase in seafood intake was also seen in participants following this anti-inflammatory dietary pattern, a source of n-3 fatty acids [29]. In line with these results, findings of another study that aimed to summarize the association between fish consumption and dietary n-3 polyunsaturated fatty acids (PUFAs) with IBD risk illustrated a robust positive correlation between n-3 PUFAs intake and decreased UC risk. However, no significant association was found between diet fish consumption [30]. n-3 PUFAs, which are anti-inflammatory, can be considered a prebiotic as they produce short-chain fatty acids (SCFA), mainly butyrate, and prevent gut dysbiosis while restoring eubiosis. The ratio of Firmicutes/Bacteroidetes resembles dysbiosis, in which Bacteroides are proinflammatory. It has been shown that administration of either a low dose (0.4 g/kg/day) or high dose (1 g/kg/day) eicosapentaenoic acid/docosahexaenoic acid leads to restoring the ratio of these species in the long term [31]. Another study revealed that n-3 supplementation was protective against the risk of preterm birth in women with a low n-3 status at baseline. However, if n-3 supplementation was given to women with a normal baseline status, the risk of preterm birth increased. Pregnant women should be carefully monitored to reduce the likelihood of preterm birth since prenatal supplementation has become more widespread nowadays [32].

Flavonoids

Flavonoids, specifically Quercetin and Rutin, which are found in many fruits like apples, grapes, citrus fruits, and berries, and vegetables like onions, broccoli, and tea, have been studied in UC patients. They have antioxidant, anti-inflammatory, immune modulating, mast-cell stabilizing, and free-radical scavenging properties, as shown in animal studies. They have also been shown to have minimal adverse health effects and can even be used with other drugs [33]. Quercetin has also been proven to show positive results in managing hypertension (pre-eclampsia) during pregnancy and spontaneous abortion by having anti-inflammatory, antioxidant, and cell-signaling modulation properties [34,35].

Berberine and Turmeric

Berberine, an isoquinoline alkaloid derived from Captis Chinesis, is widely used in traditional Chinese medicine. It has been found to have therapeutic effects on UC, including excellent anti-inflammatory and anti-bacterial effects. A journal article has shown that berberine protects the epithelial barrier of the intestine in UC. It achieves this by selectively enriching bacterial flora, producing SCFA, stimulating fermentation, increasing the amount of bifidobacteria that protect the intestinal mucosa, and improving intestinal porosity [36]. Furthermore, berberine has been used to restore reproductive health in women with polycystic ovary syndrome (PCOS) by regulating insulin resistance, unstable glucose levels, and lipid metabolism. Although human studies have not yet been conducted, in vitro and animal studies have shown promising effects of berberine in reducing inflammation [37].

Similarly, turmeric, with its bioactive component curcumin, also exhibits therapeutic properties. Curcumin has antioxidant, anticoagulant, and anti-carcinogenic properties that prevent inflammation [31]. When the effects of Bromelain and Turmeric were analyzed in an animal-based study, it was found that the combination of both substances had a synergistic mechanism that decreased inflammation in UC. In line with these results, curcumin capsules were also found to be a beneficial herbal treatment for reducing the duration and severity of dysmenorrhea, a severe condition that causes pain before or during a period [38].

Pregnant women are at a higher risk for many diseases, including COVID-19. Studies have investigated the relationship between safe, low-dose curcumin supplementation in pregnant women and the prevention of COVID-19. Pregnant women are chosen as candidates for developing COVID-19 because their bodies experience increased inflammation in the first and third trimesters, and the secretion of proinflammatory cytokines such as IL-1B, IL-6, and TNF-a is significantly increased in COVID-19 patients. Findings reveal that curcumin suppresses the release of proinflammatory cytokines, acts as an antioxidant by scavenging oxidative molecules, and helps maintain anticoagulant levels when given at doses of 0-3 mg/kg/day recommended by the World Health Organization to prevent liver or kidney issues. Other advantages of curcumin are its effectiveness in herbal treatment, affordability, and easy availability over the counter. Therefore, it is necessary for governments, healthcare workers, and the community to spread this information and promote agribusiness [39].

Probiotics

Probiotics have numerous beneficial health effects, such as normalizing gut flora, reducing bloating, balancing immune responses, and strengthening gut barriers. They are widely used in managing UC. Among the most studied probiotic strains are Bifidobacterium longum, Lactobacillus plantarum, Lactobacillus acidophilus, and Bifidobacterium lactis. These strains have shown various positive health effects in UC patients, including decreased plasma C-reactive protein (CRP) levels, reduced drug use and hospitalization, and most importantly, maintaining remission and improving the gut microbiome [40]. Probiotics have also been used as an alternative therapy for preserving fertility, pregnancy, and menopause. It has been confirmed that the primary probiotic strain that can restore the microbiome of the vagina is Lactobacillus, as it inhibits the growth of harmful bacterial strains and maintains homeostasis in the vagina. Fertility has been improved in PCOS women after supplementing with Lactobacillus, as reductions in inflammatory cytokines such as IL-6 and CRP have been observed [41].

Dietary Fiber

Although epidemiological studies have associated a fiber-rich diet, including whole grains, fruits, and vegetables, with a reduced risk of unpleasant pregnancy and birth effects, many Australian women consume insufficient dietary fiber during pregnancy [42]. Based on a cohort study (n=208), only 29.5% of women met the recommended intake for dietary fiber of 29 grams

daily. The Australian Dietary Guidelines recommend consuming two fruit portions and five servings of greens every day during pregnancy, but it has been demonstrated that only approximately 4% of pregnant patients meet these recommendations each day [43]. Another study has revealed that a high-vegetable diet, including various colored peppers and vegetables such as tomato, onion, and olive pickles, protects IBD patients [22]. Fruits, cereals, and vegetables contain phytochemicals (lignans, flavonoids, and antioxidants) that exert antioxidant effects, maintain intestinal integrity, and have anti-inflammatory effects through growth factors [44].

Vitamin D

Since the majority of UC patients have malnutrition, the absorption of certain nutrients and vitamins, especially iron and vitamin D, can be affected. A study has shown that supplementing with a dose of 40,000 IU of vitamin D for eight weeks decreases the expression of inflammatory markers in both the circulation and intestine of patients with active UC [45]. In terms of female reproductive health, serum levels of 25 (OH)D greater than 50 nmol/L have been significantly correlated with a higher likelihood of successful pregnancy following in vitro fertilization treatment, as it stimulates the production of estrogen and progesterone. Supplementation of 400 IU of vitamin D daily is recommended for all pregnant women, even before conception, but higher amounts are required for women deficient in vitamin D, primarily 800 IU [46].

Another aspect of the benefits of vitamin D on women's health is menopause. Low levels of vitamin D are correlated with increased secretion of parathyroid hormone (PTH) in postmenopausal women. Therefore, supplementing with vitamin D reduces PTH levels and increases levels of 25(OH)D, which helps prevent osteoporosis. Elevated PTH levels can lead to high calcium levels in the blood, resulting in bone thinning and increased bone porosity. However, women who are not deficient in vitamin D will not experience additional benefits from supplementation. Therefore, the decision to supplement should be based on individual needs. Body Mass Index (BMI) is a crucial indicator of vitamin D deficiency, and studies have shown that supplementing can reduce levels of triglycerides and insulin in postmenopausal women [47]. Previous studies have also found a positive association between vitamin D deficiency and an increased risk of pregnancy, childbirth, and postpartum-related complications such as low birth weight, premature birth, and repeated pregnancy loss. Therefore, vitamin D deficiency is an independent factor that increases the risk of IBD disease activity [48].

Conclusion

In conclusion, this review provides substantial evidence of the multifaceted impact of UC on women throughout various stages of life, including puberty, sexuality, fertility, pregnancy, lactation, and menopause. It also highlights the relationship between diet and susceptibility to UC symptoms. The active phase of the disease significantly exacerbates UC symptoms, particularly during pregnancy. Concerns about adverse outcomes during pregnancy and for the baby have led women to delay conception or discontinue treatment, demonstrating the significant influence of disease activity.

The positive association between UC and inflammation is evident through elevated levels of proinflammatory markers such as CRP, TNF-a, and IL-6. Therefore, an anti-inflammatory diet that emphasizes a high intake of dietary fiber from fruits, vegetables, and whole grains is an optimal strategy for maintaining disease remission and preventing adverse health outcomes in women with UC.

Early diagnosis of UC should prompt regular checkups, at least every six months, to monitor for deficiencies and maintain consistent levels of inflammatory cytokines. Preventing malnutrition and nutritional deficiencies is crucial as they can worsen disease symptoms. Therefore, it is imperative to implement nutritional education programs for women with UC, regardless of symptom severity, to prevent future complications.

To strengthen the foundation for future research, it is recommended to include a more diverse and representative sample of the general population. This should include women of all ages diagnosed with UC, both outpatients and inpatients, and individuals from different income levels in both urban and rural settings. Additionally, increasing sample sizes and the number of studies in specific investigations is necessary to ensure the validity and reliability of results. It is also important to mitigate biases, such as recall, selection, and publication biases. Prospective research methods should be prioritized over retrospective approaches to enhance the robustness of data collection.

Future investigations should explore the nuanced relationship between different dietary patterns and their impact on UC symptoms in women. Furthermore, the association between assisted reproductive techniques, conception methods, and disease course should be further examined. Shedding light on contemporary dietary trends and approaches for treating UC in women should be a focal point for future research endeavors.

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