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Published in:
Journal of Crohn's and Colitis

DOI:
10.1093/ecco-jcc/jjac189

Journal of Crohn's and Colitis, 2023, **17**, 663–680
https://doi.org/10.1093/ecco-jcc/jjac189
Advance access publication 20 December 2022
ECCO Topical Review

Multidisciplinary Perinatal Care in IBD

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Abstract

Background and Aims: Patients with inflammatory bowel disease [IBD] are often affected during their reproductive years and may have many perinatal queries that require the comprehensive perspectives of a multidisciplinary team [MDT]. The purpose of this topical review is to assess the scientific evidence and provide expert opinion related to nutritional, psychological and supportive care of women and their infants throughout the prenatal, antenatal and infant periods.

Methods: A consensus expert panel of a paediatrician, gastroenterologists, nurses and dietitians was convened by the European Crohn's and Colitis Organisation. This panel critically reviewed literature related to the non-medical management of patients with IBD during preconception, pregnancy, the postnatal period and the first years of the infant's life. Statements were developed using an e-Delphi process over two rounds and were confirmed when ≥80% of experts agreed with the statements.

Results: A total of 19 current practice positions were developed that cover the preconception period, pregnancy and lactation, and early-life exposures associated with risk of IBD. Development of the infant microbiome and its role in the immune system and topics including nutritional optimization, psychological support and education relating to early life were reviewed.

Conclusions: Patients with IBD have unique nutritional and psychosocial needs that may affect fertility and pregnancy outcomes. The early-life environment of infants born to parents with IBD may be associated with subsequent development of IBD in offspring. An MDT is the optimal setting to support and counsel patients throughout the perinatal period.

Key Words: Pregnancy; nutrition; inflammatory bowel disease; dietitian; IBD nurse; psychologist

1. Introduction

Inflammatory bowel disease [IBD], including Crohn's disease [CD] and ulcerative colitis [UC], is a multifactorial, immune-mediated disease that requires lifelong management. Patients with IBD are often affected during their reproductive years.[1] Active disease during preconception and pregnancy is associated with adverse pregnancy outcomes, including preterm delivery, low birth weight [LBW] and small for gestational age [SGA].[2–5] Furthermore, prenatal, perinatal and postnatal life factors that are linked to changes in the infant gut microbiota may have roles in determining the long-term health of the infant into adulthood.[6] There is currently a lack of robust evidence on perinatal holistic management in IBD, as pregnant or breastfeeding women are often excluded from clinical

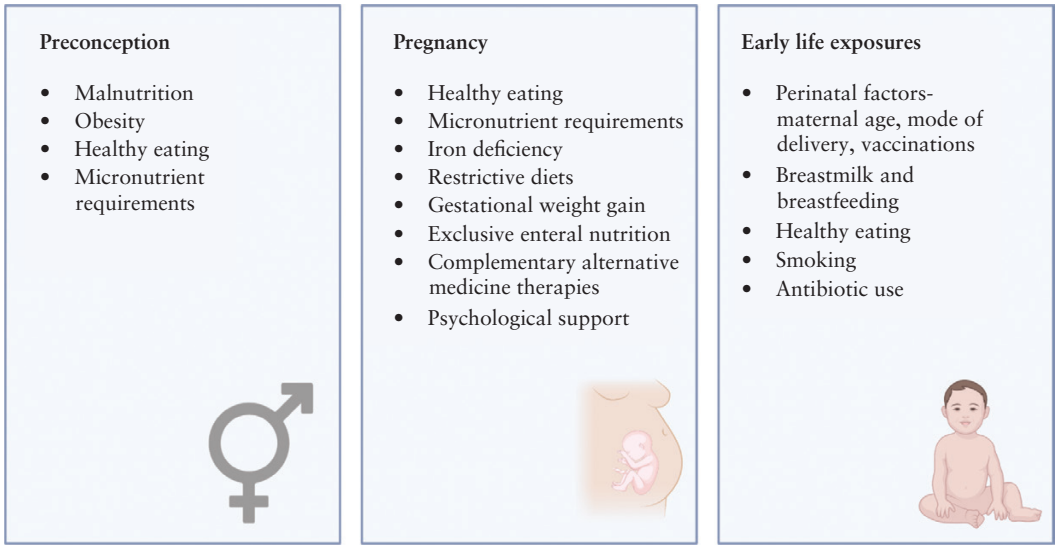

Figure 1. Multidisciplinary Perinatal Care in IBD. Created with BioRender.com.

trials. While guidelines on the management of IBD in pregnant women exist,[7,8] there are currently no publications that guide clinicians through the non-medical management of women with IBD who are planning a pregnancy, during pregnancy, or after pregnancy or for the first years of the infant's life.

The perinatal period raises many concerns beyond medical therapy that can be addressed by the IBD multidisciplinary team [MDT]. These include diet and nutrition to improve fertility and pregnancy outcomes, psychological health, safety of complementary alternative medicine [CAM] therapies, and education on environmental factors, including microbiome factors, which may be associated with IBD onset in the offspring.

The purpose of this topical review is to review the scientific evidence and provide expert opinion related to the nutritional, psychological and supportive care of women and their infants throughout the prenatal, antenatal, postnatal and infant periods (Figure 1).

2. Methods

European Crohn's and Colitis Organisation [ECCO] topical reviews are intended to provide guidance in clinical areas where scientific evidence is lacking and are developed from expert opinion consensus informed by literature reviews. Fifteen ECCO members were selected based on their expertise and allocated into four working groups [WGs]. Each WG included a gastroenterologist, IBD nurse and dietitian to represent the diverse perspectives of the MDT. WG1 covered epigenetics and microbiome development, WG2 covered preconception, WG3 covered pregnancy and WG4 covered early-life development. All WGs focused on the non-medical aspects of perinatal MDT care of patients with IBD. The working groups searched for studies with appropriate keywords published in PubMed, Medline, Scopus and Embase. Searches were restricted to studies published in English. The search terms and article selection process for each practice point are provided as supplementary materials. A total of 20 provisional practice positions were initially generated. Practice positions that reached >80% agreement during online voting were considered as final. The remaining practice positions were refined during a virtual consensus meeting held in July 2022 and then subjected to a vote. One provisional practice point was ultimately rejected. The remaining 19 practice points appear in this document.

3. Results

3.1. Development of the infant microbiome and its role in the immune system

A complex community consisting of 10–100 trillion organisms exists within the adult gastrointestinal tract. Although there may be some *in utero* acquisition of microbiota by the foetus, a rapid influx of microbiota to the infant is observed soon after birth.[9–11] These bacteria are largely derived from the mother.[12] Within a few days of birth, the diversity of the infant gut microbiota becomes markedly reduced.

For the first few weeks of life, the genetic makeup of the infant strongly influences the composition of the gut microbiota. However, the gut microbiota continues to evolve and environmental factors become the strongest determinant of its composition.[13] Strains originating from the maternal gut are most likely to become persistent and to form the stable gut microbiota in the offspring.[12] Later in childhood, some maternally derived strains may be replaced by strains from the environment [including strains acquired from other family members].[14–16] The gut microbiota evolves during the first years of life and is believed to remain relatively stable thereafter.[17] However, recent literature suggests that the gut microbiota may continue to evolve throughout childhood.[18–20]

Most data on the role of the microbiome in the development and maturation of the immune system are derived from animal models. Development of the foetal immune system begins in the first trimester.[21] Birth marks a transition from an immune system that supports maternal–foetal tolerance to one in which the processing of pathogens becomes developed.[22–24] This early postnatal immune development occurs in response to gut commensals. There is an expansion of B cells

and promotion of switching from a foetal Th2 phenotype to a Th1 or Th17 phenotype.[23] A modulation of regulatory T-cell homeostasis occurs in response to short-chain fatty acids, a by-product of bacterial fermentation.[25]

3.1.1. IBD epigenetics; microbiome influences of maternal IBD

Although a family history of IBD is a strong risk factor for IBD development, genetic susceptibility explains only a small proportion of the heritability of IBD. The gut microbiome diversity of pregnant women with IBD and their offspring is reduced compared to control mothers and their babies. A greater abundance of pro-inflammatory Proteobacteria and a reduced abundance in beneficial Bifidobacteria is observed. In a humanized experimental mouse model, these microbiome alterations affect the development of the immune system.[26] Similarly, a longitudinal study showed higher faecal calprotectin levels and abundance of *Alistipes* in babies born to mothers with IBD compared with healthy mothers, suggesting an altered microbiome and subclinical inflammation in early life.[3] Immuno-protective breast milk components, such as sIgA, are also reduced in mothers with IBD, while pro-inflammatory cytokines, lactate and succinate are increased, potentially impacting the gut microbiome and inflammatory condition of their infants.[27] Lastly, abnormal vaginal microbiota were more frequently observed in pregnant women with IBD when compared with a non-IBD-matched control group.[28] Other studies in murine models indicate that lifelong changes in the immune system occurring in response to early-life variation in microbiota predispose to certain illnesses.[29] These observations, together with other data indicating the dominance of maternally derived strains in an offspring's stable gut microbiota, suggest a potential mechanism for the microbial epigenetic inheritance of IBD.

3.1.2. IBD epigenetics; antibiotics and infections

Antibiotics and infections are important factors that may affect microbiome development and promote dysbiosis.[30] There are also some studies that examined the possible link between antibiotic exposure and infections [in the pre- and perinatal period and in early life] and the risk of developing IBD in later life.[31–43] Unfortunately, the general quality of the data related to IBD is low, with a limited number of mainly prospective case-cohort studies with heterogeneous protocols. It remains unknown if this association is true and if drug-induced dysbiosis is a key aetiological mechanism. Nevertheless, some evidence from animal studies is available. For example, Miyoshi *et al*. confirmed that peripartum administration of antibiotics led to persistent intestinal dysbiosis, which increased the risk of immune dysfunction and developing IBD in a murine colitis model.[44]

These observations are important, as 20–25% of pregnant women receive antibiotics.[45] A recent meta-analysis showed that neonates from mothers exposed to antibiotics in the peripartum period are characterized by decreased microbial diversity, with a reduced abundance of Bifidobacteria and Bacteroidetes and increased abundance of Proteobacteria.[45] Nevertheless, these data may be biased by several confounding factors, such as mode and time of delivery or feeding methods. Less is known about the possible influence of antibiotics given earlier in pregnancy on microbiota development.

The association between exposure to antibiotics in early life and increased risk of developing IBD is more established.[31,37] Animal studies suggest hypothetical mechanisms for this association, including microbiota perturbation together with disturbances in intestinal epithelial cell maturation and specific immune dysfunction, such as reduced presence of Th17 lymphocytes in the small intestinal lamina propria.[46–49]

3.1.3. IBD epigenetics; dietary influences and microbiome

Although limited evidence exists regarding the role of perinatal diet in IBD aetiopathogenesis, breastfeeding remains the strongest protective dietary factor for IBD risk. A recent systematic review of 35 studies showed a dose-dependent association and maximal decrease in offspring IBD risk when breastfed for at least a year compared to ≤6 months.[50] A register-based national cohort study from Denmark also showed lower odds for IBD among offspring of mothers exposed to increased vitamin D levels via mandatory fortification of margarine when compared with controls unexposed during the entire pregnancy.[51] In the absence of more evidence including patients with IBD, non-IBD human studies have proposed perinatal dietary factors that should be further investigated. A study of 267 non-IBD mother–child pairs showed that environmental toxins and chemical exposure through breast milk can alter microbiome function during the critical period of infancy, although the potential impacts on child health and IBD risk remain unknown.[52] Maternal fish oil supplementation during pregnancy and breastfeeding led to increased breast milk eicosapentaenoic acid and greater abundance of *Bifidobacterium* and *Lactobacillus* in the stools of their infants.[53] Probiotic supplementation during pregnancy does not seem to alter the microbial composition or diversity in children 2 years following birth.[54]

Studies on first-degree relatives of patients with CD indicate that impaired intestinal barrier function is associated with later development of CD[55] and altered microbial composition and function, including reduced alpha diversity.[56] Interestingly, an analysis of long-term dietary habits indicated that a Mediterranean-like dietary cluster was associated with increased abundance of fibre-degrading bacteria [such as *Faecalibacterium*] and with lower faecal calprotectin levels of first-degree relatives of patients with CD.[55] On the other hand, exposure to 15 g/day of the emulsifier carboxymethyl cellulose [CMC] in healthy subjects resulted in altered microbiota composition towards reduced diversity and invasion into the sterile inner mucus layer,[57] a phenomenon that was previously associated with the development of colitis in a predisposed murine model.[58] Further research is needed to evaluate whether diet–microbiome interactions play a role in modifying disease risk in first-degree relatives of patients with IBD.

Extensive evidence from animal models of gastrointestinal inflammation also implicates diet–microbiome interactions in IBD development. A maternal high-fat diet and maternal obesity is associated with an altered microbiome, increased susceptibility in models of intestinal injury, mucosal neutrophil infiltration and intestinal permeability in rodent offspring.[59–63] Similarly, an imbalanced maternal intake of n-6/n-3 polyunsaturated fatty acids led to offspring dysbiosis, increased susceptibility to dextran sulfate sodium (DSS) and dinitrobenzene sulfonic acid colitis, and reduced survival post *Citrobacter rodentium* challenge. In contrast, milk fat appears to be protective against offspring enteric infection risk.[64–67] Similar dysbiosis and gastrointestinal damage effects were induced by maternal P80 intake,[68] maternal

Table 1. Perinatal counselling topics

Topic	Specific examples
Contraception	Planned pregnancy enables disease activity and nutritional status to be optimized prior to conception
Nutrition	Perinatal nutrient supplementation, nutritional status screening, importance of food and nutrition on outcomes of both mother and baby
Inheritance	Risk of inheritance differs according to parental IBD status
Fertility	Impact of IBD on fertility differs according to factors such as disease activity and surgical history
Medication management	Most medications used in IBD are safe before conception and in pregnancy. Individualized discussion is necessary particularly for medications not regarded as safe, such as methotrexate
Disease activity and management	Importance of disease control prior to conception and during pregnancy. At least 3 months of steroid-free remission prior to conception is ideal
Pregnancy flare management plan	IBD team develops a plan in consultation with the patient and obstetrics
Delivery	Developed by obstetrics and the patient in consultation with IBD team as required
Mental health assessment and management	There is increased risk of mental health disorders in IBD, particularly in pregnancy and post-partum
Multidisciplinary consultations	Input of a multidisciplinary team, including a dietician, colorectal surgeon and psychologist is recommended
General health promotion	Avoidance of smoking, alcohol consumption and recreational drug use
Health maintenance	Regular colonoscopies for dysplasia surveillance if indicated, cervical smears, skin checks and vaccinations
Other considerations	History of previous abdominal surgery, presence of stoma and other non-IBD co-morbidities

IBD, inflammatory bowel disease.

methyl-donor supplementation,[69,70] and a phyto-oestrogen-enriched diet.[71] On the other hand, maternal butyrate supplementation increased the diversity of the gut microbiome in the offspring and prevented gut injury.[72] A maternal polyphenol-enriched diet during pregnancy and lactation can prevent offspring dysbiosis in a murine model of UC predisposition.[73] Combined maternal and neonatal administration of the probiotic *Lactobacillus rhamnosus* GG increased offspring bodyweight gain, mucosal IgA production and colonic microbiome diversity, and decreased susceptibility to DSS colitis.[74] These findings should be replicated by human IBD studies before any clinical practice conclusions can be drawn. The MELODY trial is an ongoing study that includes dietary interventions that aim to modulate the microbiome of mothers with CD before delivery, reduce risk of maternal relapse during this critical period, and prevent gut inflammation and autoimmune disease risk in their offspring.[75] The results of this trial and further studies of similar designs are required to elucidate the role of diet–microbiome interactions in IBD epigenetics.

3.2. Preconception period

3.2.1. Multidisciplinary counselling

Current Practice Position 1.1

Preconception counselling at the time of diagnosis in patients of child-bearing age and ideally in the preceding 3 to 6 months prior to attempts at conception is recommended. Counselling is best delivered in a multidisciplinary setting

Models of care for delivery of preconception counselling in IBD have been reported in the literature and include topics shown in Table 1. Reported outcomes from dedicated preconception education include improved patient knowledge, medication adherence, quality of life and reduction in voluntary childlessness.[76–79] Furthermore, a reduction in active disease during pregnancy and reduction in the risk of SGA infants has also been observed.[80] Models by which preconception counselling can occur include use of a single outpatient clinic session, an intensive series of outpatient clinic appointments leading up to conception and educational interventions, such as an online educational portal or a patient-centred decision aid.[76,77,80,81]

Existing pregnancy guidelines, recommendations and studies assessing the role of preconception counselling suggest a multidisciplinary setting, with involvement of representatives from gastroenterology, obstetrics, colorectal surgery, IBD nursing, psychology, dietetics and midwifery.[8,79,82,83]

Included in the multidisciplinary delivery of counselling is the discussion and assessment of dietary habits and nutrition in pregnancy in general[84] and specifically in relation to IBD. Nutritional risks include the potentially detrimental impact of active disease, history of surgical resection and behavioural patterns that negatively impact diet quality.[85,86] Furthermore, women with IBD are at risk of inadequate gestational weight gain, which is associated with adverse consequences such as SGA infants.[87,88] While there are limited data on the continuation or initiation of nutritional therapies in pregnancy, such as exclusive enteral or parenteral nutrition, the available data are supportive.[89,90] The potential for adverse reproductive outcomes associated with nutritional compromise in IBD is also applicable to men, including the impact of malnutrition on male fertility.

3.2.2. Fertility and malnutrition

Current Practice Position 1.2

There is a high prevalence of malnutrition in IBD, and poor nutritional status in women and men is associated with infertility. Nutritional screening and management of deficits is important in the preconception period

Undernutrition in the general population can lead to a higher risk of infertility.[84] Malnutrition is common in IBD,

Table 2. Perinatal nutritional requirements and supplementation

	Preconception and pregnancy recommendations	Rationale
Iron	Supplement prior to conception if deficient and supplement with 30–60 mg/day during pregnancy if at risk of deficiency	Women with IBD are at higher risk of iron deficiency. Iron stores should be monitored 3–6 months before conception and throughout pregnancy. A supplement should be taken accordingly. If oral iron is not tolerated, IV iron may be administered in the second and third trimester but monitoring for adverse reactions is recommended
Calcium	While taking corticosteroids, supplementation with 800–1000 mg/day calcium and 800 IU/day vitamin D is recommended. Supplementation may be required if calcium intake from food is low	If dairy or high-lactose products are avoided and a calcium-fortified plant-based alternative is not used, a referral to a dietitian for an assessment and/or supplementation is recommended
Vitamin D	Supplementation with 400 IU/day or 2000 IU/day if deficient is recommended. Upper safe limit in pregnancy is 4000 IU/day	Women with IBD are at a higher risk of vitamin D deficiency. Vitamin D status should be assessed 3–6 months prior to conception and supplemented accordingly. Adequate status in pregnancy ensures that the baby is not deficient at birth
Folate	Supplementation with 800 µg/day for at least 4 weeks before and 12 weeks after conception is recommended	A higher folic acid dose and/or continuing folic acid supplementation throughout pregnancy is recommended if there is a history of folate deficiency, a gluten-free or low-fibre diet is followed, a history of small-bowel resection or moderate-to-severe small bowel Crohn's disease, the patient is taking sulfasalazine, or combinations thereof
Vitamin B12	Screen for deficiency before conception and during pregnancy. Appropriate supplementation is recommended if deficient or likely to become deficient. Women already taking a monthly vitamin B12 supplement can continue this throughout pregnancy	Women with IBD are at higher risk of deficiency, especially if they have had >20 cm of ileum resected, avoid consumption of animal products or both
Iodine	A 150 µg/day supplement during pregnancy is recommended in some countries. Local guidelines should be consulted	In some countries, women have low iodine status due to low soil iodine concentrations, low iodine concentrations in food or both
Fibre	Consumption of 25–30 g/day before conception and throughout pregnancy is recommended	Consuming fibre from various foods groups helps manage pregnancy-related constipation. A diet that includes whole foods rich in fibre is associated with positive pregnancy outcomes for mother and baby. Insoluble dietary fibre may need to be modified to reduce obstructive symptoms in those with fibrostenotic stricturing disease
Energy and protein	Energy and protein requirements are increased during pregnancy and lactation [+70, +260, +500 kcal/day for the first, second, and third trimester, respectively, and +500 kcal/day during breastfeeding]. Underweight or active disease may increase requirements	Protein energy malnutrition is common in women with IBD, especially in patients with active disease, surgical history or who avoid certain foods. If energy and protein requirements are not met from a regular diet, oral nutritional supplements may be considered.

IBD, inflammatory bowel disease; IV, intravenous.

in particular protein energy malnutrition in CD, with prevalence rates differing between inpatient and outpatient settings.[91] In a Spanish prospective, multicentre study using subjective global assessment, 16% of outpatients were malnourished. A history of abdominal surgery, active disease and avoidance of certain foods during flares were associated with a higher risk of malnutrition.[92] In a recent prospective, multicentre, observational study assessing the validity of the Global Leadership Initiative on Malnutrition [GLIM] in IBD, 238 hospitalized patients were enrolled of whom 60.1% were malnourished, with patients with CD significantly more malnourished than those with UC [69.5% vs 32.8%, $p < 0.001$].[93] Given the prevalence of malnutrition, routine malnutrition screening is recommended. Table 2 outlines the recommendations for nutritional screening in the preconception period. If screening reveals risk, contributing factors should be investigated and addressed, with referral to a dietitian for malnutrition treatment. Furthermore, preconception counselling with a dietitian may mitigate the risk of malnutrition or nutrition-related disorders and help improve nutritional status pre-pregnancy.[94]

There is no evidence that inactive UC and CD affect fertility in men and women in the absence of pelvic surgery.[7,95–101] However, males with CD may be at risk of poorer semen quality and lower zinc levels.[96,100] Patients with IBD are generally recommended to follow a balanced diet while in remission. However, nutritional screening and assessment for micronutrient deficiencies is recommended on a regular basis.[94]

3.2.3. *Fertility and obesity*

Current Practice Position 1.3

Obesity is an increasing concern in the IBD population. Given the potential detrimental impact of obesity on fertility, foetal development and pregnancy outcomes, support should be provided to assess and address obesity in patients who are considering pregnancy

It is known that obesity negatively impacts female and male fertility.[102–105] Several studies have shown that weight

loss in women with a body mass index [BMI] in the obese range is associated with a significant improvement in pregnancy rates.[106–111] The prevalence of obesity is increasing in the IBD population,[94] and varies between countries from 17 to 35%.[94,112,113] Cross-sectional studies indicate that 15–40% and 20–40% of adult IBD patients in Western countries are obese or overweight, respectively.[114] Obesity may be associated with obstetric complications in the general population. However, it is important to avoid rapid weight loss or restrictive or 'fad diets' before conception or during pregnancy. Such diets can lead to micro- and macronutrient deficiencies with negative consequences.[84] Pregnant women who are overweight or obese should be encouraged to eat a healthy diet, avoid non-nutritive, energy-dense foods and engage in regular physical activity.[84] Referral for specialist weight management input should be considered in patients with chronic conditions.[103] For patients who require bariatric surgery, consensus recommendations suggest postponing pregnancy after bariatric surgery to ensure maximal weight loss, weight stabilization, and to reduce the risk of macronutrient and micronutrient deficiencies and electrolyte imbalances.[102] Bariatric surgery may also negatively impact male fertility in the short term, which may be induced by the release of lipophilic toxic substances due to rapid weight loss.[104]

3.2.4. Healthy eating

Current Practice Position 1.4

Preconception counselling is suggested to include promotion of healthy eating to promote adequate energy and nutrient intake

There is limited IBD-specific evidence regarding preconception nutritional requirements for foetal development. However, there are general recommendations for improvements in nutrition and health status both before and during pregnancy, as there are associations with optimal foetal growth, obstetric outcomes, and perinatal survival and better long-term health in the mother and child.[84]

A diet with a balanced macronutrient intake that includes ample vegetables, fruits, whole grains, nuts, legumes and healthy fats is generally recommended. A healthy diet usually limits intake of simple sugars, processed foods, and trans- and saturated fats. For example, in non-IBD populations, a preconception Mediterranean diet has a positive effect on fertility in both men and women.[115–117] This diet includes a high intake of vegetable oil, fish, legumes and vegetables.[117] Conversely, diets high in glycaemic load, carbohydrate-to-fibre ratio and added sugar are associated with modestly reduced fecundity.[118]

3.2.5. Micronutrient status

Current Practice Position 1.5

Micronutrient status should be screened and corrected annually in patients with IBD and specifically in the 3 to 6 months prior to attempts at conception

Nutritional deficiencies are common in IBD.[119–123] Iron deficiency is present in one in three IBD outpatients and anaemia in every fifth,[119,121,124,125] with higher rates in inpatients. Anaemia is often multi-factorial, with causes including impaired small-bowel absorption due to inflammation, extensive small-bowel resection, increased losses and/or inadequate dietary intake.[119,126] Folate deficiency can affect 20–60% of people with IBD.[127] In the Swiss IBD Cohort, folate deficiency was observed in 92% of patients with CD and 94.6% with UC.[121] Vitamin B12 deficiencies affect 4.3–26.6% of patients and are more common in those who have had terminal ileum resections.[119,121–124] Vitamin D deficiencies have been observed in 16–95% of IBD patients.[120,128,129] Vitamin D levels are also lower in the pregnant IBD population.[125] Vitamin D deficiency in IBD is associated with increased disease activity.[83] Beyond the impact of IBD, many factors affect vitamin D levels, including skin pigmentation, sunlight exposure, living in latitudes above 40°, colder seasons, older age and sunscreen use.[130] Vitamin D deficiency may impact female fertility.[131,132] Adequate maternal vitamin D levels are also needed for foetal stores that are used in the first months of life.[133] Vitamin D supplementation in pregnancy is likely to reduce the risk of pre-eclampsia, gestational diabetes and low birthweight and may reduce the risk of severe postpartum haemorrhage.[134]

Women with IBD are more likely than the general population to be deficient in key micronutrients that are required in increased amounts in early pregnancy.[101] During the preconception period, it is recommended that women with IBD are monitored for folate, iron, vitamin B12 and vitamin D deficiency.

Folic acid supplementation is recommended for at least 4 weeks prior to conception and continued for the first 12 weeks of gestation to reduce the risk of neural tube defects.[7,94,135,136] Dietary folate intake is often low and a daily dose of 800 µg is recommended. However, supplementation of up to 4–5 mg/day may be required in specific situations [Table 2]. Maintenance of serum iron and ferritin levels within the normal range is recommended.

There is no consensus for optimal vitamin D supplementation in IBD and in deficiency.[137] There is limited evidence from animal and human studies suggesting that fertility may be impaired in females with low vitamin D levels. Furthermore, decreased vitamin D levels in the preconception phase may increase the risk for adverse pregnancy outcomes. Accordingly, screening for 25(OH)D deficiency and appropriate supplementation is recommended.[138,139]

3.3. Pregnancy and lactation

3.3.1. Multidisciplinary care

ECCO Current Practice Position 2.1

A joint pregnancy clinic with a dedicated gastroenterologist, obstetrician and IBD nurse is advised for the management of women with IBD. A comprehensive multidisciplinary team that includes a dietitian and psychologist with IBD expertise can provide optimal support

Pregnant women with IBD should be managed by a coordinated approach between the gastroenterologist and the obstetrician to ensure consistent advice is provided, including IBD medical therapy.[76,140,141] The IBD nurse specialist has a fundamental role in liaising with the gastroenterologist and obstetrician whilst supporting the patient with timely monitoring to minimize IBD flares and facilitate prompt intervention as needed.[82]

Dedicated IBD–obstetric antenatal clinics are associated with higher compliance to medical treatments and better pregnancy outcomes.[142,143] Counselling and education during pregnancy should include information regarding the low risk of most IBD medications during pregnancy and the high risk of a significant disease flare during pregnancy in case of medication interruption.[144] However, this model of care is not currently routine. A survey of 97 UK IBD units revealed that IBD–obstetric antenatal clinics were well established in only 14% of units.[145] There are some published examples of comprehensive IBD perinatal management. The 'IBD MOM Clinic' at the Shaare Zedek Medical Center [Israel][146] includes gastroenterologists, obstetricians, an IBD nurse, a dietitian and a psychologist. Pregnant women with moderate-to-severe IBD activity are seen at the 'IBD MOM Clinic' and have similar perinatal outcomes as women in remission or with mild disease activity.[146]

Finally, biological and emotional changes occurring during pregnancy and the perinatal period may reveal subclinical psychiatric conditions in women with IBD and should not be neglected by health providers.[147]

Therefore, a joint clinic including a gastroenterologist, obstetrician and IBD nurse dedicated to care of pregnant women with IBD is advisable. The addition of a dietitian with expertise in IBD and a psychiatrist or psychologist to the team is recommended for optimal support. This clinic may also ensure that women receive adequate postpartum care and support to initiate and continue breastfeeding. In addition, this environment can be used to educate new parents with IBD about early-life exposure that may increase the risk of their offspring developing IBD [see section 3.4].

3.3.2. Psychosocial support

ECCO Current Practice Position 2.2

Pregnant women with IBD report a high level of pregnancy-related concerns and fear of negative pregnancy, maternal and foetal outcomes related to IBD and IBD medication. Non-judgemental psychosocial support should be offered by clinicians to obtain a favourable pregnancy outcome for mother and baby

Pregnant women with IBD report a high level of pregnancy and maternal concerns. These relate to potential harmful effects of medication on their unborn child or baby, receiving conflicting advice from their general practitioner, obstetric team or both regarding IBD and IBD medication, passing IBD onto their baby or their children developing IBD in the future, harmful effects of pregnancy on their IBD, and dietary concerns during pregnancy.[148–152]

To address these concerns, clinicians should guide and educate the patient regarding the optimal time to conceive, discuss the safety of medications and any risks, and together decide on the best management strategy to achieve a good outcome. Proactively addressing pregnancy-related beliefs of IBD patients can significantly reduce pregnancy-related concerns and anxiety and depression symptoms and improve pregnancy knowledge and medical adherence.[149,153] This may be achieved through an e-health portal[153] or a single educational intervention with women with IBD who wish to conceive.[149]

Pregnant women with IBD should be supported and counselled on the safety and importance of therapy adherence in maintaining remission. Where necessary, women should be followed up as high-risk obstetric patients. Optimal management requires an interdisciplinary team effort, involving the IBD team in collaboration with obstetricians and the general practitioner.[154]

Consistent, ongoing follow up should reduce anxieties and fears surrounding IBD medications during pregnancy, thus providing the optimal conditions for expectant mothers to achieve their goal of having a healthy baby and having the same overall well-being as women without IBD.

3.3.3. Healthy eating

ECCO Current Practice Position 2.3

Pregnant women with IBD should be encouraged and advised to eat a healthy diverse and balanced diet, rich in nutritious foods, in accordance with specific national recommendations

The association between maternal dietary patterns and pregnancy outcomes has been investigated in healthy women.[155–161] Although somewhat inconsistent, studies have found that high consumption of vegetable oils, fruits, vegetables, whole grains and fish were protective against adverse pregnancy outcomes, including preterm birth and SGA.[158,159] Adherence to the Mediterranean diet pattern was inversely associated with a range of adverse pregnancy outcomes for both mothers and offspring.[162] A randomized controlled trial in women at high risk for SGA found that a Mediterranean diet reduced the incidence of SGA compared with usual care recommendations.[163] Conversely, a diet low in vegetables, fruit and whole grains and high in processed and refined foods is associated with a higher risk of SGA.[159] Ultra processed food [UPF] intake during pregnancy is associated with gestational weight gain [GWG] and neonatal body fat.[164]

The only study to date that has assessed the effect of dietary patterns on pregnancy outcomes in women with IBD [183 CD, 240 UC] is the Norwegian Mother and Child Cohort Study [MoBa]. This study revealed that a traditional dietary pattern that included fish and fish products, gravy, potatoes, rice porridge and cooked vegetables was associated with a lower risk of SGA.[86]

Like the healthy population, pregnant women with IBD should be advised to eat a diverse and healthy diet. This should include a variety of vegetables, fruits, whole grains, nuts, legumes, fish and oils high in monounsaturated fat. Intake of red meat and refined grains, simple sugars, processed foods, and trans and saturated fats should be restricted.[84,165,166] A dietitian should be consulted about any special dietary considerations or food intolerances to ensure adequate dietary and nutritional intake.

3.3.4. Prevention and treatment of micronutrient deficiencies

ECCO Current Practice Position 2.4

Pregnant women with IBD are at risk for micronutrient deficiencies and should be screened in the first trimester for folate, iron, vitamin B12 and vitamin D deficiencies. If deficient, dietary counselling, supplementation and monitoring should be provided accordingly

Pregnant women with IBD are at a higher risk of micronutrient insufficiencies and therefore micronutrient status should be monitored preferably each trimester, with dietary counselling and supplementation provided accordingly. Improving nutritional status prior to or during pregnancy is associated with improved health of the mother and offspring.[84]

Screening for nutritional deficiencies may be suboptimal in patients with IBD. A UK survey of 97 IBD centres on preconception, pregnancy and postpartum care of women with IBD found that the only micronutrient routinely discussed was folic acid.[145]

Recommended multivitamin supplements for pregnant women vary between countries. Women should be encouraged to follow at least local recommendations for healthy women to reduce pregnancy-related complications.[8] Due to the higher prevalence of micronutrient deficiencies in non-pregnant women with IBD, some women with IBD may need a longer duration or higher doses of supplementation [Table 2].

Vitamin D deficiency is highly prevalent in pregnant women with IBD. A cross-sectional study revealed that 50.8% of pregnant women with CD and 60.9% of pregnant women with UC were vitamin D-deficient compared with 17.4% of healthy pregnant women, with an adjusted relative risk ratio for vitamin D deficiency of 2.98 (95% confidence interval [CI]: 2.19–4.04) for CD and 3.61 [95% CI: 2.65–4.93] for UC.[125] In women with deficiency, vitamin D supplementation is associated with lower rates of pre-eclampsia, preterm delivery and LBW.[167] Vitamin D supplement recommendations during pregnancy vary among guidelines of nutrition in pregnancy,[168] but most guidelines recommend a supplement of at least 400 IU/day.[168] Higher doses of 2000 IU/day for 8 weeks may be considered if vitamin D deficiency is present.[125,129]

Calcium supplementation is recommended in patients with low dairy or calcium intake.[168] Pregnant women treated with corticosteroids should be advised on routine calcium and vitamin D supplementation to prevent steroid-associated loss of bone mass.[83]

Folate deficiency is common in IBD, as is vitamin B12 deficiency in those with a previous ileal resection.[121] In the general pregnant population, adverse birth outcomes were observed in a large retrospective cohort of women with an imbalance in folate and vitamin B12 status.[169] The prevalence and impact of such an imbalance in pregnant women with IBD is not known. Pregnant women with IBD should be screened for micronutrient status at least during the first trimester and treated accordingly. Women with low dietary intake of folate, a history of folate deficiency or both should be advised to continue folic acid supplementation throughout pregnancy.[8,170] According to the European Society of Parenteral and Enteral Nutrition [ESPEN] guidelines, women with CD who have had a resection >20 cm of distal ileum are at risk for vitamin B12 deficiency and should routinely be administered prophylactic vitamin B12.[94]

3.3.5. Prevention and treatment of iron deficiency

ECCO Current Practice Position 2.5

Iron deficiency is common in pregnant women with IBD. Therefore, counselling to increase intake of iron-rich foods is recommended. An elemental iron supplement of 30–60 mg/day throughout pregnancy is recommended for women at risk of iron deficiency. Iron stores should be monitored at the beginning of every trimester and supplementation discussed accordingly

Iron deficiency is common during pregnancy as iron requirements increase. Low haemoglobin is associated with adverse pregnancy outcomes, such as premature delivery and maternal and child mortality.[171] Iron deficiency may alter the child's development both *in utero* and later in life.[171] Thus, the World Health Organization recommends supplementation of 30–60 mg/day of elemental iron for all pregnant women as early as possible.[171] In a retrospective analysis of electronic databases, iron deficiency was common and found in 22/33 of pregnant patients with IBD, mostly in the third trimester when iron requirements substantially increase. Recognition and treatment of iron deficiency was more common in patients attending a tertiary referral centre when compared with external IBD care.[172] In patients with IBD, a proactive approach of early detection and treatment of iron deficiency regardless of anaemia is recommended.[173] Patients with IBD may be reluctant to take an oral iron supplement as it may cause worsening of gastrointestinal symptoms.[174] Patients should be counselled on the benefits of adequate iron status or trials of alternative iron preparations should be discussed. Pregnant women with IBD should be screened for iron deficiency every trimester and oral iron supplementation prescribed if they are deficient or at risk of becoming deficient. If oral iron is not tolerated, intravenous [IV] iron may be administered in the second and third trimester, although the risks and benefits to the mother and foetus should be thoroughly considered.[175,176] A case report of foetal bradycardia in a 24-year-old patient with active CD following IV administration of iron suggests that CD patients may be predisposed to adverse reactions to IV iron.[177]

3.3.6. Restrictive diets and eating practices

ECCO Current Practice Position 2.6

Restrictive diets, restrictive eating practices and/or avoidance of specific food groups may cause nutritional inadequacy and deficiencies and should be used with caution in women with IBD. Screening for suboptimal dietary patterns and subsequent referral to an IBD dietitian is recommended

Micronutrient and energy requirements during pregnancy are increased. In healthy non-IBD women, increased dietary intake to meet energy requirements usually ensures increased nutrient intake. However, in women with IBD, avoidance of particular foods to manage symptoms during both active and quiescent IBD is common.[178,179] This may result in lower caloric-protein intake and inadequate micronutrient intake, which in turn may contribute to deficiencies.[179,180]

Elimination diets used in IBD care (such as the low FODMAP [fermentable oligosaccharides, disaccharides, monosaccharides and polyols] diet) are restrictive by nature and may lead to nutritional deficiencies and dietary inadequacy.[181] Such diets are not routinely recommended unless under dietitian supervision. A retrospective study evaluated the safety of a dietitian-led elimination diet in 34 pregnant women with CD to investigate whether such diets affect pregnancy outcomes. No differences were observed in the frequency of miscarriage, stillbirth, congenital abnormality, premature delivery, LBW or need for Caesarean section.[182]

It is recommended to screen for restrictive eating practices during perinatal clinic appointments. Screening may include asking questions about current dietary intake and whether specific foods or food groups are avoided. Specific screening tools may be used once widely available. Women following restrictive diets or avoiding particular food groups should be referred to an IBD dietitian for further nutritional assessment and intervention to promote adequate nutritional intake.

3.3.7. Inadequate gestational weight gain

ECCO Current Practice Position 2.7

Inadequate gestational weight gain in patients with IBD should be considered as an independent risk factor for adverse neonatal outcomes. Counselling with support from a dietitian to promote adequate weight gain is recommended

Adequate GWG is dependent on pre-pregnancy BMI[183] and is essential for foetal development and growth. In the general pregnant population, inadequate GWG is associated with maternal and neonatal complications, including SGA and LBW.[184] The data suggest a similar association in women with IBD. In a retrospective analysis of 75 pregnant patients with IBD and 225 controls, SGA and preterm delivery were more frequent in patients with IBD, and GWG < 12 kg was significantly associated with adverse pregnancy outcomes.[185] A retrospective examination of a clinical birth database that included 212 patients with IBD revealed that pregnant IBD patients had a higher rate of newborns with growth retardation (odds ratio [OR]: 2.12; 95% CI: 1.29–3.50) and Caesarean section [OR: 2.74; 95% CI: 1.81–4.13].[186] In the pregnancy IBD and neonatal outcomes cohort [PIANO],[88] women with inadequate GWG had a 2.5-fold increased risk of preterm birth compared with pregnant women who gained sufficient weight [CD, OR: 2.5; 95% CI: 1.30–4.90 and UC, OR: 2.5; 95% CI: 1.20–5.60]. In women with CD but not UC, there was a 3-fold increased risk of intrauterine growth restriction and a trend for SGA in women with inadequate GWG. The inclusion of active disease in the adjusted models did not change the association, suggesting that inadequate GWG in women with IBD may be due to factors other than disease activity, and this can strongly influence the risk of preterm birth.[88]

The prospective population-based Norwegian mother and child cohort found that inadequate GWG in women with a BMI of 18.5–25.0 kg/m^2 occurred significantly more often among women with CD [39%] and UC [33%] than in non-IBD women [21%].[87] Furthermore, the risk of infants being SGA was 4.5 and 5.5 times higher in women with CD and UC with inadequate GWG, respectively, than in women with adequate GWG. Active disease during pregnancy occurred in approximately a third of women with adequate [35.1%] and inadequate GWG [36.8%]. When added to the regression models, this did not influence the association between inadequate GWG and adverse pregnancy outcomes. This suggests inadequate GWG is an independent predictor of SGA[87] and should be monitored in pregnant women with IBD. When inadequate GWG is observed, disease activity should be considered and evaluated in addition to referral to a dietitian for nutritional optimization.

3.3.8. Exclusive enteral nutrition

ECCO Current Practice Position 2.8

Exclusive enteral nutrition is safe and useful in inducing remission in pregnant women with CD. Dietitian counselling and monitoring is pivotal to ensure nutritional adequacy when using diet as a treatment strategy to induce remission in women with IBD

Exclusive enteral nutrition [EEN] is recommended to induce CD remission in adults when corticosteroids are contraindicated, as may be the case during pregnancy.[83] Use of EEN to induce remission during pregnancy has been rarely reported. One retrospective study reported that 12/14 pregnant women with CD treated with EEN achieved disease remission and delivered healthy, full-term babies.[89] It is important to assess the vitamin A content of the EEN formulas. Excess intake of vitamin A as retinol [but not β carotene] is teratogenic and is associated with an increased risk of congenital malformations.[187]

3.3.9. Complementary and alternative therapies

ECCO Current Practice Position 2.9

The effects of most complementary and alternative [CAM] therapies during preconception, pregnancy and lactation have not been studied. Therefore, the MDT should assess the safety data for all CAM therapies taken by pregnant women with IBD. Initiation of new CAM therapies in pregnant women with IBD is not recommended

The use of CAM by patients with IBD is common.[188] To date, there are insufficient data on the impact of alternative medicine [including dietary supplements such as curcumin, probiotics, herbal mixes] on pregnancy outcomes and foetal development,[189] especially in the high doses that may be recommended for non-pregnant women with IBD. Healthcare providers should ask all pregnant women with IBD about their use of CAM, and the risks and benefits of each product in pregnancy should be discussed.[190] For example, there are limited data suggesting that fish oil supplements may help prevent preterm birth [prior to 34 weeks].[166] Another example is curcumin, which is often used to treat UC.[188] Although there is increasing interest in curcumin during pregnancy, the safety of curcumin preparations, especially in the doses commonly used in UC, has not been established in pregnancy.[191,192]

3.4. Early life and risk of IBD development

3.4.1. Perinatal factors

ECCO Current Practice Position 3.1

There is no clear association between mode of delivery, maternal age, perinatal factors, vaccinations and the subsequent risk of developing IBD

Several studies have evaluated the role of perinatal factors on the risk of chronic diseases and their potential impact on early microbiome composition.[193,194] Specifically, the risk for immune-mediated disorders may be secondary to low exposure to toll-like receptor-2 [TLR-2] tolerizing bacterial

products with reduced immune regulation[195,196] A few studies reported a slightly higher risk for IBD in children born by Caesarean section or with other perinatal factors [e.g. prematurity, birth order, LBW].[197,198] Similarly, reports on the association between vaccination and IBD risk reported null results.[199] A recent meta-analysis evaluated the role of prenatal and perinatal environmental factors on the risk of developing IBD and did not reveal any significant correlation between perinatal factors [maternal or paternal age, maternal diseases during pregnancy, LBW, premature weight, birth order, birth month and latitude] and IBD risk.[31]

3.4.2. Breast milk and breastfeeding

ECCO Current Practice Position 3.2

Breast milk provides ideal nutrition, has positive effects on the immune system of the newborn and may protect against development of IBD

Several meta-analyses of observational studies suggest that breastfeeding is associated with a reduced risk of IBD.[31,200–202] The ESPEN guidelines concluded in favour of breastfeeding as the optimal food for infants, stating that it reduces the risk of IBD by offering protection against gastrointestinal infections due to its ability to stimulate development of the gastrointestinal mucosa and its immunological capacity in children.[94] A meta-analysis of 35 relevant articles revealed that breastfeeding has a protective role against the risk of developing UC and an even greater role against CD.[203] Apart from providing nutrition and protection against infection for the newborn, the researchers concluded that breastfeeding protects against development of CD and UC in children and disease onset in adults. Even if infants are breastfed for only a short period of time, the risk of CD is significantly increased when compared with infants who are breastfed for a longer time [≥12 months].[50] Current European recommendations state that breastfeeding should be continued as long as mutually desired by both mother and infant.[94]

3.4.3. Healthy eating

ECCO Current Practice Position 3.3

To reduce the risk of IBD development, children should be provided with a balanced, diverse and age-appropriate diet that meets local healthy eating dietary recommendations. These dietary patterns usually include a variety of vegetables, fruit, whole grains, nuts and seeds, and legumes, and a moderate amount of animal products. Limiting intake of ultra-processed foods is recommended

Several prospective studies in adults have consistently demonstrated that animal protein is associated with an increased risk for UC.[204–206] Consistent with this, a large Dutch cohort recently revealed that a carnivorous dietary pattern comprising red meat, poultry and processed meat was associated with an increased incidence of UC [OR: 1.11; 95% CI: 1.01–1.20].[207] Furthermore, a Western dietary pattern was associated with an increased incidence of CD [OR: 1.16; 95% CI: 1.03–1.30].[207] On the other hand, a Mediterranean diet is widely promoted as a healthy dietary pattern with anti-inflammatory effects and is associated with a reduced CD risk.[208] In addition, fibre intake, particularly from fruits, was associated with incident CD, but not UC.[209]

In children, specific foods such as vegetables, fruits, fish and nuts were associated with a lower risk for CD.[210] A case-control study in Canadian children also confirmed that a dietary pattern rich in fruit and vegetables [prudent diet] was associated with a decreased risk for CD, while a partial 'Western diet' increased the risk for CD.[211] Furthermore, it may be beneficial to reduce intake of UPF and food additives such as emulsifiers, thickeners and preservatives as much as possible, as increased intake of UPF has recently been linked to IBD onset.[212,213] Overall, evidence suggests that a balanced and diverse diet that meets local healthy eating dietary guidelines is likely to reduce the risk of IBD development.

3.4.4. Smoking

ECCO Current Practice Position 3.4

Maternal smoking during pregnancy may be associated with development of IBD in the offspring. There is no clear association between passive smoking in children during early life and development of IBD

Parental passive smoking during pregnancy is associated with increased IBD risk in the offspring. A case-control study in South-East Scotland revealed that parental smoking during pregnancy and around birth was more common in parents of IBD cases than control parents [OR: 2.87; 95% CI: 1.23–6.66].[214] Maternal smoking during pregnancy and at birth was more common with IBD cases than in controls [OR: 4.46; 95% CI: 1.16–17.1] and in mothers of patients with CD [OR: 4.23, 95% CI: 1.05–16.97].[214] Data on passive smoking early in life are less clear, although a trend to an increased risk has been shown in several studies.[31,200]

3.4.5. Antibiotic use

ECCO Current Practice Position 3.5

There is no clear association between antibiotic exposure during pregnancy and subsequent risk of developing IBD in the offspring. Early-life exposure to antibiotics and the number of antibiotic courses may increase the risk of developing IBD. Early-life enteric and non-enteric infections, specifically otitis media, may increase the risk of developing IBD

Approximately 20–25% of women receive antibiotics during pregnancy.[45] A recent meta-analysis by Agrawal *et al.* found two cohort studies showing an increased risk of developing IBD among children exposed to antibiotics during pregnancy [OR: 1.8; 95% CI: 1.2–2.5].[31]

Early use of antibiotics and IBD risk has been evaluated in several studies, with a general trend confirming a possible role [mainly in the first year of life] and a correlation with the number of antibiotic courses.[215] A recent systematic review revealed an association between early-life antibiotics and IBD,[37] although a meta-analysis on three studies did not find a clear relationship between antibiotic use in infancy and risk of IBD.[31] A nested case-control study showed that four or more antibiotic courses in the first 6 or 12 months of life are associated with IBD risk [OR: 6.34; 95% CI: 1.68–24.02 and OR: 2.91; 95% CI: 1.31–6.45, respectively].[33] This effect may be

due to antibiotic-mediated altered composition of the human gut microbiota. Many studies have evaluated the impact of enteric and non-enteric infections early in life and the risk of developing IBD. A recent systematic review and meta-analysis reported a positive association between early infections, specifically otitis media, and IBD risk,[31] specifically CD.[41,42] A Canadian nested case-control study of a population-based database that matched 294 children with IBD to 2377 controls based on previous diagnosis of otitis media revealed that children with an otitis media diagnosis by 5 years of age were 2.8-fold [95% CI: 1.5–5.2] more likely to be an IBD case. The authors speculated that the diagnosis of otitis media could be an indirect measure of antibiotic use.[41] In addition, a Swedish cohort study reported that gastrointestinal infection combined with antibiotic therapy was associated with a higher risk of IBD than infection alone.[216] It is biologically plausible that both factors may alter the gut microbiome, possibly contributing to the pathogenesis of IBD.[200]

4. Discussion

Most pregnancy and IBD guidelines focus predominantly on perinatal medical management.[8,217] The purpose of this review is to provide evidence-informed expert opinion to guide clinicians on the nutritional, psychological and supportive care of women and their infants throughout the prenatal, antenatal, postnatal and infant periods.

Despite the paucity of prospective IBD-specific perinatal evidence, there is increasing evidence in non-IBD populations that perinatal nutritional status and lifestyle of both parents are associated with perinatal outcomes. Much of the existing evidence is applicable to the IBD population. In addition, evidence is accumulating for the role of perinatal and early-life exposures in epigenetics and in shaping the gut microbiota. Therefore, the perinatal period is probably a critical window of opportunity to improve health outcomes of the infant, with a potential to modify IBD risk.

Poor nutritional status is common in patients with IBD and may include malnutrition, obesity, nutritional deficiencies, unhealthy eating patterns or combinations thereof. Nutritional status affects fertility in both women and men, and optimizing nutritional status prior to conception may improve pregnancy outcomes for mothers and their infants. Correction of nutritional deficiencies [such as iron] may be challenging during pregnancy; therefore, a proactive approach aiming for nutritional sufficiency prior to conception is recommended. Controlling disease activity and ensuring adequate GWG during pregnancy require close monitoring by the MDT. Importantly, as pregnant women are often excluded from clinical trials, data on the safety of dietary and CAM therapy are limited and therefore vigilance is recommended, except for EEN therapy that can be offered instead of steroids in a subset of patients with active CD.

As fear and anxiety are common in patients with IBD, psychosocial and supportive care are crucial to improve patient quality of life. Perinatal counselling should also include parental education on early-life exposures that are associated with risk of IBD. Breastfeeding and healthy lifestyle habits can benefit mothers and their infants and should be promoted during the perinatal period.

This review highlights the important role of the MDT. A perinatal MDT that includes a dedicated gastroenterologist, obstetrician, IBD nurse, dietitian and psychologist with IBD expertise is suggested. This setting is likely to provide optimal care, education and support to prospective and current parents with IBD and their infants.

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Conflict of Interest

ECCO has diligently maintained a disclosure policy of potential conflicts of interests [CoI]. The conflict of interest declaration is based on a form used by the International Committee of Medical Journal Editors [ICMJE]. The CoI statement is not only stored at the ECCO Office and the editorial office of JCC, but is also open to public scrutiny on the ECCO website [https:// www.ecco-ibd.eu/about-ecco/ecco-disclosures.html], providing a comprehensive overview of potential conflicts of interest of authors. The ECCO Topical Review Projects are based on an international consensus process. Any treatment decisions are a matter for the individual clinician and should not be based exclusively on the content of the ECCO Topical Reviews. ECCO and/or any of its staff members and/or any consensus contributor may not be held liable for any information published in good faith in the ECCO Topical Reviews.

Acknowledgements

We thank the ECCO Office, especially Fadi Ifram and Martina Baeva, for their support and guidance in preparing this topical review.

Author Contributions

This manuscript is a joint expert consensus activity. Hence all authors participated sufficiently, intellectually or practically, in the work to take publicresponsibility for the content of the article, including the concept, design, data interpretation, and writing of the manuscript. The final version of the manuscript was approved by all authors.

Funding

This work was supported by the European Crohn's and Colitis Organisation.

Supplementary Data

Supplementary data are available online at *ECCO-JCC* online.

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