

Preconception, antenatal and postpartum management of inflammatory bowel disease



CPD 

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Background

Inflammatory bowel disease (IBD), comprising ulcerative colitis and Crohn's disease, commonly affects individuals of childbearing age. Pregnancy in women with IBD presents an anxiety-provoking prospect for practitioners and patients alike, with disease flares occurring in between 20% and 55% of patients antenatally.

Objective

The aim of this review is to provide an overview of antenatal IBD management principles and therapeutic goals, with a specific focus on the role of general practitioners.

Discussion

A collaborative approach is favoured in managing pregnancy and IBD. Preconception counselling should be prioritised, with emphasis on the importance of achieving three months of preconception corticosteroid-free remission. Close monitoring of disease activity in pregnancy is crucial, warranting the careful interpretation of both clinical and biochemical parameters. Reassurance regarding the safety of IBD medications in pregnancy and vaginal delivery can be provided in the majority of cases. Specialist support should be sought expeditiously in the setting of disease flare, particularly where symptoms and biochemical parameters are refractory to escalation of 5-aminosalicylates or topical therapies, corticosteroids or biologic agents are required, or an emergent IBD complication is suspected.

INFLAMMATORY BOWEL DISEASE (IBD), comprising ulcerative colitis (UC) and Crohn's disease (CD), commonly affects women of childbearing age.¹ Both UC and CD are immune-mediated, relapsing and remitting chronic inflammatory disorders predominantly affecting the gastrointestinal tract. In the majority of cases, IBD is treated with immunomodulatory therapies for induction and maintenance of disease remission (Table 1).

Australia has one of the highest rates of IBD in the world, with a prevalence of more than one in 300.² Greater than 50% of patients are diagnosed with IBD prior to 35 years of age, and more than 25% of affected women conceive for the first time following their IBD diagnosis.^{2,3} General practitioners (GPs) are integral to the ongoing health maintenance of patients with IBD. Patients see their GPs as frequently as their IBD specialists in the six months post original diagnosis, and up to one-third of patients with IBD are managed exclusively by a primary care physician.^{4,5} Furthermore, onset of IBD in pregnancy is occasionally encountered.^{6,7} Accordingly, the aim of this article is to provide an evidence-based review of the approach to and management of patients with IBD prior to, during and following pregnancy.

Preconception counselling and goals

As for all individuals, those with IBD planning a pregnancy should receive preconception counselling focusing on behavioural, nutritional and health maintenance interventions (Table 2).⁸⁻¹¹ The prospect of pregnancy may be associated with anxiety in women with IBD, resulting in an increased rate of voluntary childlessness.¹² Women with IBD express concerns regarding the potential impact of their medical therapies and disease on fertility, timing of pregnancy, risks of flaring in pregnancy and the effect of a flare and medication use on the fetus.^{12,13} A single gastroenterologist-led preconception educational intervention can improve patients' anxiety and depression

levels and pregnancy-related knowledge and enhance medication adherence¹³ while reducing the risk of IBD relapse.¹⁴ Online pregnancy in IBD decision aids have also been shown to improve pregnancy in IBD-related knowledge in both the preconception period and during pregnancy.¹⁵ Detailed preconception counselling can be delivered via a face-to-face consultation, via telehealth review or using online resources.¹⁶ In those who fall pregnant without having received preconception counselling, an early antenatal appointment to provide this education is warranted (Table 2).

Fertility does not appear to be adversely affected in women with well-controlled IBD but may be decreased in the setting of severely active or complex penetrating disease, as well as in those with extensive prior surgical resections or low body mass index (BMI).^{8,17} Referral for fertility specialist review should be considered within 6–12 months of unsuccessful attempts at conception, particularly in those with prior surgical interventions. If required, in-vitro fertilisation is purported

to be equally as effective for patients with IBD as for those without IBD.¹⁸ However, those with prior CD-related surgery or a failed ileal pouch–anal anastomosis (IPAA) may have reduced live birth rates with assisted reproductive technology.¹⁹

Compared with those in remission, patients with active IBD in pregnancy have a greater than three-fold increased risk of spontaneous abortion, low birth weight infants and preterm delivery, as well as an increased risk of stillbirths.^{6,20} IBD activity should hence be subjectively and objectively assessed prior to conception, with preconception disease control essential to minimising the risk of antenatal IBD flares. Of those in clinical remission, approximately one-third will experience a flare in pregnancy, compared with 55% of those with active disease at the time of conception.²¹ Thus, three months of corticosteroid-free clinical and biochemical, cross-sectional imaging or endoscopic remission is recommended prior to attempting conception.⁸ With regards to medications, thiopurine metabolites (6-thioguanine

and 6-methylmercaptopurine) should be checked prior to conception and monitored throughout pregnancy because of the associated increased risk of intrahepatic cholestasis of pregnancy.²² In those receiving allopurinol in combination with a thiopurine, gastroenterological input should be sought prior to conception because of potential teratogenicity.²³ Biologic medications should be continued throughout conception and pregnancy (Table 3).⁸

Concerns regarding IBD heritability are commonly cited by patients with IBD wishing to conceive.¹³ The risk of IBD developing in a child born to a mother with IBD varies according to ethnicity but is reassuringly low at approximately 1.6–4.1% for UC and between 2.7% and 4.8% for CD.^{24,25} IBD risk can be as high as 30% in those with both parents affected by IBD.²⁶

Antenatal management

Given the risks associated with disease flare, women with IBD require close monitoring during pregnancy. Assessment

Table 1. Medications safely used in pregnant patients with inflammatory bowel disease

Medication class	Medication names	Route of administration	Dosing frequency	Mechanism of action
Aminosalicylates	Sulfasalazine, mesalazine, balsalazide, olsalazine	Oral and per rectal	Daily	Local colonic anti-inflammatory effects
Thiopurines	Mercaptopurine, azathioprine	Oral	Daily	Decrease DNA replication in highly proliferative cells, including lymphocytes
Anti-tumour necrosis factor (TNF) antibodies	Infliximab, adalimumab, golimumab	Intravenous (IV) and/or subcutaneous (SC)	Adalimumab – every 1–2 weeks Infliximab – every 4–8 weeks IV, every two weeks SC Golimumab – every four weeks	Immunoglobulins that neutralise soluble and membrane-bound TNF, a pleiotropic pro-inflammatory cytokine
Anti-integrin antibody	Vedolizumab	IV or SC	Every 4–8 weeks IV, every two weeks SC	Prevents lymphocyte trafficking to the gastrointestinal mucosa by blocking integrin $\alpha 4\beta 7$
Anti-interleukin (IL) 12/23 antibody	Ustekinumab	SC	Every 4–8 weeks	Blocks the shared p40 subunit of pro-inflammatory cytokines IL12/23
Corticosteroids	Prednisolone, budesonide	Oral and per rectal	Daily	Binds to intracellular receptors and modulates expression of multiple pro-inflammatory genes

in each trimester, including in those in remission, is recommended.⁸ Biochemical assessment is particularly important, as symptoms of active IBD are difficult to differentiate from those that can occur as a consequence of other pregnancy complications, such as haemorrhoids.^{7,27}

Furthermore, routine inflammatory markers are affected by pregnancy and must be interpreted with consideration for appropriate pregnancy reference ranges.²⁷ Contrastingly, faecal calprotectin remains accurate in pregnancy and can additionally be used to evaluate those

with symptoms potentially attributable to new-onset IBD, such as rectal bleeding and diarrhoea.^{7,28} In the latter context, a faecal calprotectin ≥ 50 $\mu\text{g/g}$ should prompt expedient gastroenterological referral for consideration of endoscopy or imaging.⁷

Table 2. Preconception counselling and health maintenance for women with inflammatory bowel disease

Nutritional supplementation	<ul style="list-style-type: none"> • Check iron, vitamin B12 and folate prior to and during pregnancy. Replace to normal range. Intravenous iron is safe in pregnancy if oral supplementation is not tolerated or inadequate.⁶ • 2–5 mg daily of folate is needed in the setting of extensive ileal disease, in those on a fibre-restricted diet and in those taking sulfasalazine for three months prior to conception and in the first 12 weeks of pregnancy.
Weight management	<ul style="list-style-type: none"> • BMI >30 kg/m^2: 5–10% body weight reduction prior to conception in order to decrease the risk of adverse obstetric outcomes such as stillbirth.⁹ • BMI <18.5 kg/m^2: dietitian intervention and IBD optimisation prior to conception with the aim of normalising BMI to mitigate the risk of infertility and intrauterine growth restriction.
Behavioural	<ul style="list-style-type: none"> • Smoking and alcohol cessation • Education regarding timing of ovulation and intercourse • Ensure up-to-date cervical screening and mammography. In those receiving immunosuppressive medications, three-yearly cervical screening should be considered.¹⁰
Contraception	<ul style="list-style-type: none"> • Preference for long-acting, non-oestrogen containing contraception in patients with active IBD, given the theoretical risk of venous thromboembolism.⁸ • Education that there is no increased risk of IBD flare with the use of oral contraceptives.⁹ • Reassurance that absorption of oral contraceptives is maintained in those with mild UC or short ileal resections.⁹ • Recommendation for non-oral contraceptives in the setting of prior extensive small bowel resection or active small bowel inflammatory disease.⁸
Vaccination	<ul style="list-style-type: none"> • Influenza vaccination • Hepatitis B, human immunodeficiency virus, syphilis, MMR and varicella serology • Vaccinate all with necessary non-live vaccines⁹ prior to pregnancy. • Live vaccination (MMR) in immunosuppressed patients (receiving thiopurines, biologics or corticosteroids long term) must be tailored to individual risk profile with infectious disease specialist input.
IBD activity	<ul style="list-style-type: none"> • Three months of corticosteroid-free remission • Clinical (assess symptoms) • Biochemical (aim for faecal calprotectin <100–250 $\mu\text{g/g}$), normalisation of C-reactive protein • Quiescent disease on cross-sectional imaging if available (intestinal ultrasonography, magnetic resonance imaging) • Endoscopic assessment may be warranted if there is discrepancy between clinical symptoms and biochemical or radiological assessment.
Medication review	<ul style="list-style-type: none"> • Corticosteroid dependence warrants gastroenterology assessment prior to conception. • Review and cease teratogenic medications (Table 3) with gastroenterological input regarding commencement of safe alternatives.
Education regarding IBD in pregnancy	<ul style="list-style-type: none"> • Significance of active disease in pregnancy • Symptoms and signs of disease flare and advice as to when to seek medical assistance • Heritability of IBD • Safety of breastfeeding • Mode of delivery • Fertility and safety of assisted reproductive technology if required • Risk of postpartum mental health issues

BMI, body mass index; IBD, inflammatory bowel disease; MMR, measles, mumps and rubella; UC, ulcerative colitis

Table 3. Preconception, antenatal and postpartum management of medications in inflammatory bowel disease

Medication	Male fertility	Female fertility	Pregnancy	Commencement for management of flare in pregnancy*	Breastfeeding
Aminosalicylates	Switch to an alternative three months prior to conception attempts	Continue, but use 5 mg daily of folic acid with sulfasalazine	Continue, but use 5 mg daily of folic acid with sulfasalazine	For mild-to-moderate flare of UC. Can commence or dose escalate both topical (enemas or suppositories) and oral formulations.	Continue, but use 5 mg daily of folic acid with sulfasalazine prior to and during pregnancy. Avoid sulfasalazine in breastfeeding.
Thiopurines	Continue	Continue	Continue	Not recommended	Continue
Methotrexate	Continue ⁴¹	Cease at least three months prior to conception	Contraindicated	Contraindicated	Contraindicated
Corticosteroids	Continue	Aim for three months corticosteroid-free remission prior to conception	Avoid prolonged (>6 week) courses or use as a maintenance agent	For moderate-to-severe UC and CD flares, or if inadequate response to aminosalicylates. Commence prednisolone 40 mg daily, weaning by 5 mg weekly, with early gastroenterology assessment. Budesonide controlled release may be trialled.* Avoid prolonged (>6 week) courses and monitor for side effects (glucose intolerance, psychiatric).	Continue at doses <40 mg prednisolone daily
Anti-TNF biologics	Continue	Continue	Continue throughout pregnancy ¹⁰	For moderate-to-severe flares of UC and CD; can be commenced in pregnancy with specialist supervision.	Continue
Ustekinumab	Continue	Continue	Continue throughout pregnancy ¹⁰	Minimal safety data for induction available.	Continue
Vedolizumab	Continue	Continue	Continue throughout pregnancy ¹⁰	Minimal safety data for induction available.	Continue
Tofacitinib	Continue	Cease at least four weeks prior to trying to conceive	Contraindicated	Contraindicated	Contraindicated

*Budesonide controlled release has been used in small bowel CD in pregnancy with no consequent adverse events, but overall safety data are extremely limited. CD, Crohn's disease; TNF, tumour necrosis factor; UC, ulcerative colitis

A faecal calprotectin of >250 µg/g in pregnancy is associated with increased risks of adverse obstetric outcomes irrespective of clinical symptoms.²⁹ Faecal calprotectin should be measured at least

once in each trimester, including in those in clinical remission. A faecal calprotectin >250 µg/g requires consideration of therapeutic escalation and early gastroenterological review.

Where imaging is required, non-GP specialist input should be sought. Intestinal ultrasonography (IUS) performed by experienced gastroenterologists is safe, feasible and accurate in the first

and second trimesters;²⁸ however, this modality is not presently widely available beyond larger tertiary centres. Magnetic resonance imaging is favoured in later pregnancy or where IUS is not accessible.²⁷ Endoscopy can be safely performed in pregnancy where clinically indicated, such as in the assessment of disease flare where non-invasive tools are conflicting, unavailable or indeterminate.⁸ Where feasible, endoscopy should be conducted un-sedated without oral bowel preparation.^{8,30}

In addition to adhering to general dietary recommendations, pregnant women with IBD may need to increase their caloric intake in the setting of active disease, ideally guided by a specialist dietitian. Inadequate gestational weight gain is more common in those who experience an IBD flare in pregnancy and is associated with an increased risk of preterm delivery and intrauterine growth restriction when compared with the general population (Table 4).^{31,32}

IBD flares in pregnancy are more common in those with UC than CD, those who have had a flare in a prior pregnancy and those not receiving a biologic agent at conception when compared with those who are receiving a biologic.^{32,33} Management of active disease largely mirrors that in non-pregnant individuals, although with important exceptions,⁸ and will vary according to the severity of the flare, the phenotype and intestinal distribution of disease, the patient's pre-existing medical therapy and their comorbid conditions

(Table 3). Thiopurine commencement or dose escalation in pregnancy is not recommended given the slow onset of action and associated risk of liver injury.²² Prolonged corticosteroid therapy should be avoided, with preference for escalation to a biologic therapy. The latter agents can be safely commenced in pregnancy, although supportive safety data are limited.⁸ Clinical response to therapy should be assessed within 1–2 weeks after starting therapy, while biochemical response should be assessed within four weeks (Table 3). In those with active disease, increased frequency of fetal growth scans in the third trimester is recommended.⁸ Emergency review is required for individuals with acute severe colitis (>6 bloody bowel actions per day and pulse >90 bpm, temperature >37.8 °C, haemoglobin <105 g/L or C-reactive protein >30 mg/dL), suspected intestinal obstruction or perforation or perianal abscess.^{7,8}

Delivery

Vaginal delivery is safe for women with IBD except those with active perianal fistulising CD, in whom a caesarean section is recommended.^{8,34} Caesarean sections should also be recommended in the context of an IPAA, where an ileal reservoir is connected to the anus following a subtotal colectomy, given the potential risk of pouch damage and faecal incontinence following a vaginal delivery.³⁵ In all other circumstances or where uncertainty exists, mode of delivery should be dictated by obstetric indications

and patient preference in consultation with the treating gastroenterologist and colorectal surgeon.

Postpartum management

Close postpartum follow-up with clinical, biochemical and psychological reassessment is extremely important. Thirty per cent of patients experience a flare in the initial 12 months postpartum, with such flares more common in those with active disease in the third trimester, those with severe CD (in whom 30% flare in the initial six months postpartum) and those who de-escalate IBD therapy during or immediately following pregnancy.^{36,37} Additionally, the risk of new-onset postpartum mood, anxiety and substance use disorders is increased in those with IBD when compared with the general population.³⁸

Infants exposed to biologic medication in utero are advised not to receive live vaccinations before one year of age, given a previous fatal case of disseminated *Bacillus Calmette-Guérin* disease in an infant exposed to anti-tumour necrosis factor biologic agent.³⁹ The only live vaccine on the Australian immunisation schedule prior to 12 months is the rotavirus vaccine. Reassuringly, observed adverse events to rotavirus vaccine in those exposed to biologics in utero are extremely uncommon.⁴⁰

All IBD medications continued in pregnancy can also be safely continued during breastfeeding (Table 1). The levels of these medications in breastmilk are so low as to have negligible effect on infant absorption;⁸ therefore, 'pumping and dumping' to minimise exposure to medical therapies is not recommended.

Conclusion

IBD commonly affects women of childbearing age, with GPs having an integral role in preconception, antenatal and postpartum care. All patients with IBD and a wish to conceive should receive tailored preconception counselling. Immunomodulatory medications are continued to maintain disease remission antenatally in the majority of cases.

Table 4. Gestational weight gain recommendations

Pre-pregnancy body mass index (kg/m ²)	Gestational weight gain recommendation in total (kg)	Recommended weight gain per month in second and third trimester (kg)
<18.5	12.5–18	2–2.6
18.5–24.9	11.5–15	1.5–2.3
25–29.9	7–11.5	1–1.5
>30	5–9	0.8–1.2

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Monitoring nutritional status and gestational weight gain is important, and a delivery plan should be made collaboratively with the obstetric team.

Key points

- IBD commonly affects women of childbearing age.
- Preconception counselling for women with IBD is essential to improve patient satisfaction, knowledge and disease-related and obstetric outcomes.
- Control of disease activity prior to and throughout pregnancy is crucial to optimising maternal and fetal outcomes.
- The majority of IBD medications can and should be continued in pregnancy and breastfeeding.
- IBD flares in pregnancy should be managed expediently and with gastroenterologist input, particularly for those for whom corticosteroids or escalation to biologic therapy may be required.
- Vaginal delivery is safe and recommended for most women with IBD who desire it.

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Competing interests: SB has received consultation fees from AbbVie and Janssen, research grants for other investigator-driven studies/clinical trial funding from AbbVie, Janssen and Shire and has received speaker's fees from AbbVie and Janssen. EKW has received consultancy fees from AbbVie and Janssen, research grants from AbbVie and Janssen and speaker fees from AbbVie, Janssen, Pfizer and Falk.

Funding: This work was supported by a St Vincent's Hospital Melbourne Research Foundation Endowment Fund Grant, a National Health and Medical Research Council Postgraduate Scholarship, and a Crohn's and Colitis PhD scholarship and a research grant from the Gutsy Group Foundation.

Provenance and peer review: Not commissioned, externally peer reviewed.

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