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TOPIC HIGHLIGHT

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From conception to delivery: Managing the pregnant inflammatory bowel disease patient

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Abstract

Inflammatory bowel disease (IBD) typically affects patients during their adolescent and young adult years. As these are the reproductive years, patients and physicians often have concerns regarding the interaction between IBD, medications and surgery used to treat IBD, and reproduction, pregnancy outcomes, and neonatal outcomes. Studies have shown a lack of knowledge among both patients and physicians regarding reproductive issues in IBD. As the literature is constantly expanding regarding these very issues, with this review, we provide a comprehensive, updated overview of the literature on the management of the IBD patient from conception to delivery, and provide action tips to help guide the clinician in the management of the IBD patient during pregnancy.

Key words: Inflammatory bowel disease; Pregnancy; Biologics; Neonatal outcomes

Core tip: Inflammatory bowel disease affects people during their reproductive years. Many patients and physicians have concerns about pregnancy in inflammatory bowel disease (IBD), and are unsure about management of IBD during pregnancy. Women with IBD have similar fertility as the general population, with the exception of certain prior surgeries, and actives disease. This review highlights the relative safety of medications used to treat IBD during pregnancy and breastfeeding, and summarizes the updated literature for immunosuppressants and biologics. Good control of disease and clinical remission at the time of conception increases the likelihood of having successful pregnancy outcomes, and quiescent disease during pregnancy.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a group of chronic bowel diseases, including Crohn's disease and ulcerative colitis, which can affect all aspects of a patient's life. The majority of patients with IBD are diagnosed in their adolescent to young adult years. The diagnosis of IBD and the medications and surgeries used to treat IBD come with many questions and concerns about how they can affect future education and work plans, and relationship and family plans. These questions and concerns not only affect the patient, but also the health care providers who are managing the patient. In particular, the complex interaction between IBD and pregnancy is important, es-

pecially because any decisions regarding the management of the patient will not only affect her, but also her fetus. In addition, they will not only affect them currently, but may have long lasting effects.

The concerns regarding IBD and reproduction certainly play a central role in any decisions made by the patient and the physician caring for her. Many women with IBD choose not to become pregnant and to remain childless. This concept of "voluntary childlessness" has been documented in early studies that showed up to 30% of women with IBD (compared to 7% of the general population) had voluntary infertility[1]. More recent studies confirm this "voluntary childlessness" continues to be an issue, with up to 18% of childless IBD patients indicating that the decision was influenced by IBD related factors[2-4]. The five major concerns of women with IBD that have been reported by previous studies include: fertility/conception, genetics, IBD-related congenital abnormalities, medication effects on pregnant and fetus, and effect of pregnancy on IBD[3-5]. Inadequate physician knowledge regarding reproduction in inflammatory bowel disease, and lack of comfort managing pregnant IBD patients may be contributing to the medical advice component of "voluntary childlessness" seen in IBD patients. In this review, we aim to address each of these major topics of concern, in the hopes that practitioners will be better equipped with up-to-date information to use in counseling their patients.

CONCEPTION

Fertility: what are the chances of becoming pregnant?

Women with IBD have been shown to have similar fertility as the general population[1,2,6-9]. However, some studies report that Crohn's disease (CD) patients may have slightly decreased fertility[10,11], especially when their disease is active[9] or if they have adhesions from prior surgeries[10,12]. Ulcerative colitis (UC) patients can have normal fertility, however once UC patients have had a surgery, such as restorative proctocolectomy and ileal pouch anal anastomosis, they have an increased risk of infertility up to 3-4 fold[13-16]. It is hypothesized this increased infertility is due to tubal infertility from the adhesions and scarring[15,16], since UC patients who have had laparoscopic IPAA have been shown to have less adhesions[17], and lower infertility rates[18,19]. Although there have been variable reports on the infertility rates among women with Crohn's disease and ulcerative colitis, some of these differences may be attributed to voluntary childlessness. In a recent meta-analysis of eleven studies, the authors found that in women with CD, fertility was reduced 17%-44% compared to controls, but further analysis revealed this to be linked to voluntary childlessness; they did not find any reduction in fertility in women with UC[20].

Action point: In general, women with IBD have similar fertility rates as the general population. Previously reported infertility may be attributed to voluntary childlessness. Women with Crohn's disease may have decreased fertility rates when their disease is active, or if have had prior surgeries. Women with ulcerative colitis who have had pelvic surgery have decreased fertility rates.

Genetics: what are the chances of offspring developing IBD?

Earlier studies supported strong genetic risks of IBD in offspring of patients with IBD up to 13 times the general population[21,22]. When early twin studies were combined, results showed concordance ranging between 15.4% monozygote twin concordance for ulcerative colitis to 30.3% concordance for Crohn's disease[23]. Monozygote twins are born from the same zygote, so this low concordance rate suggests there are other non-genetic influences, such as environmental factors. A recent study re-ran the Swedish twin registry, which is one of the major data sources for twin studies, and found that previous twin studies overestimated the influence of genetics in Crohn's disease[24]. Although genetics does play an important role in the risk of developing IBD, they are not the only determinants.

Action point: Genetics play an important role in the risk of developing IBD, but women should be counseled that there are other factors involved. Their offspring will not necessarily develop IBD.

PREGNANCY

Conception and beyond: what is the effect of IBD activity on the pregnancy?

Some studies indicate that IBD, especially Crohn's disease, can be associated with an increase in adverse pregnancy outcomes, such as prematurity[2,10,14,25-33], low birth weight[14,25,26,28,31-32], small for gestational age[25,28,30,33,34], congenital abnormalities[28,31,35], miscarriages or spontaneous abortions[11,30]. Other studies report no significant association between IBD and adverse pregnancy outcomes[9,29,36-38]. However, the effect of IBD on pregnancy outcomes may be partially attributable to disease activity, and medications, rather than IBD alone. In addition, other demographic variables such as maternal age and smoking have been shown to be risk factors for congenital abnormalities and pregnancy outcomes such as preterm delivery, among women with IBD[38].

A few studies concluded that disease activity did not predict adverse pregnancy outcomes in women with IBD[1,30,32], but other studies found that active disease at the time of conception, and during pregnancy, increases the risk of adverse pregnancy outcomes, such as spontaneous abortion[1,6,7] and preterm delivery[37,39].

Action point: Women with IBD should be in remission before attempting to become pregnant.

Conception and beyond: what is the effect of pregnancy on IBD course?

Women with active disease at the time of conception, or

within 3 mo of conception, are more likely to have active disease during pregnancy than if their disease was in remission[40,41]. For both ulcerative colitis and Crohn's disease, the relative risk of a women having active disease during pregnancy if she had active disease at the beginning of pregnancy is about two-fold[41]. Conversely, women with disease in remission at the time of conception are more likely to have quiescent disease during pregnancy[6]. Pregnancy was reported to decrease activity of Crohn's disease in a study of 61 women[42], but a larger study including 92 women with Crohn's disease found no statistical significant difference in disease course during or after pregnancy[43]. Longer disease duration in Crohn's disease patients may increase the risk of relapse during pregnancy[43]. In ulcerative colitis patients, there was a higher risk of relapse during pregnancy and in the post partum period[43]. A large study on 543 women over 10 years reported that pregnancy was associated with a reduced number of flares in the years following pregnancy[44].

Action point: The disease activity at time of conception tends to predict disease course during pregnancy. Ideally, women should be in remission at the time of conception.

Flares and remissions during pregnancy: which medications can be used during pregnancy?

Women who require medications to achieve and maintain remission of their IBD, should continue these medications during pregnancy. With the exception of methotrexate, which should be stopped when attempting to conceive, and withheld during pregnancy, other medications used to manage IBD have not been associated with significant adverse fetal outcomes.

Aminosalicylates [Food and Drug Administration (FDA) Class B, Asacol FDA Class C] and sulfasalazine (FDA Class B): Aminosalicylates and sulfasalazine are commonly used drugs for mild to moderate ulcerative colitis. A cohort study from Denmark found an increased risk of stillbirth and preterm birth in women prescribed 5-ASA drugs during pregnancy, but was unable to distinguish between effects of disease activity and 5-ASA[36]. Other studies found no significant association between 5-ASA drugs and poor pregnancy outcomes[45-51]. A recent meta- analysis reported slight but non-significant increases in congenital malformation (OR = 1.16), stillbirth (OR = 2.38), spontaneous abortion (OR = 1.14), and preterm delivery (OR = 1.35) and low birth weight (OR = 0.93) with 5-ASA medications[51]. However, again, the results were pooled, and they were unable to differentiate which 5-ASA drug, type of disease, or disease activity. Recently there has been concern about the dibutyl phthalate (DBP) coating on certain mesalamines, as animal studies found adverse effects on development and reproductive organs[52]. A recent study reported high mean urinary concentrations of the main DBP metabolite in a woman who used Asacol[52]. However, there have been no reports of adverse developmental or reproductive effects on humans. In addition, DBP can be found in many commonly used medications and dietary supplements[53].

Sulfasalazine inhibits folate synthesis, so women on sulfasalazine should be supplemented with folic acid (5 mg/d) to prevent neural tube defects[54,55]. Sulfasalazine can also displace bilirubin from albumin, which theoretically could lead to kernicterus in the newborn child, but no cases have been reported[55].

Action point: Amniosalicylates and sulfasalazine can be used during pregnancy, and are not significantly associated with adverse neonatal outcomes. Women on sulfasalazine should receive folic acid supplementation (5 mg/d).

Azathioprine and 6-mercaptopurine/Purinethol (FDA Class D): Although thiopurines are classified as FDA Class D drugs, because of teratogenicities in animal studies, the use of azathioprine/6-MP during pregnancy in IBD is not associated with increased risk of preterm birth, low birth weight, neonatal adverse outcomes, or congenital abnormalities[33,49,56-60]. Disease activity rather than medication use can lead to neonatal adverse outcomes[57]. One study reported that thiopurines increased the risk for congenital malformations when compared to healthy women, but not when compared with IBD controls[61]. A large ongoing prospective registry of pregnancy outcomes in women with IBD exposed to immunomodulators and biologic therapy (PIANO study) has found no association with the use of immunosuppressants with congenital anomalies, abnormal newborn growth and development, or other complications[62]. In addition, a recent review found that thiopurine use during pregnancy was not associated with low birth weight or congenital abnormalities, but was associated with pre-term birth[63]. Infants may be exposed to a metabolite of Azathioprine, 6-TGN[64,65], and a recent study has found that up to 60% of infants exposed to thiopurines in utero are born with anemia[65]. In long-term (average 4 years) follow-up studies of babies exposed to azathioprine in utero, there was no increased risk of infection[66] or development and immune function[67]. Expert opinion is to continue thiopurine use during pregnancy to maintain remission of disease[54,68].

Action point: Thiopurines can be used during pregnancy, and are not significantly associated with adverse neonatal outcomes.

Methotrexate (FDA Class X): Methotrexate is a teratogen and an abortifacient, and is therefore contraindicated during conception and pregnancy period. Methotrexate exposure during organogenesis (6-8 wk) may lead to congenital abnormalities, while exposure in the second and third trimesters can lead to fetal loss[55,69]. Since Methotrexate remains in the tissue for a period of time, patients should discontinue at least 3-6 mo prior to attempting to conceive[54,69]. Women who become pregnant while on methotrexate should seek medical attention immediately, for assessment of the fetus, and counseling

regarding options[54,55].

Action point: Methotrexate should be discontinued at least 3 to 6 mo before conception.

Corticosteroids (FDA Class C): Glucocorticoids cross the placenta and can reach the fetus, but the placental enzymes convert corticosteroids to less active metabolites[54,55]. Prednisone, prednisolone, and methylprednisolone are the preferred agents during pregnancy, as they are more efficiently metabolized by the placenta than dexamethasone or betamethasone[54]. Most studies on glucocorticoid use during pregnancy have been in patients with various diseases, such as asthma. There has been a reported association of increased oral cleft in neonates exposed to glucocorticoids in utero in the first trimester, and this risk should be discussed with the patient[54,55,69]. Overall there is no increased risk of congenital abnormalities[50]. Budesonide has only been reported in one small study in Crohn's disease patients, and was not associated with adverse neonatal outcomes[70].

Action point: Corticosteroids may be used to treat flares of IBD during pregnancy. There is a small risk of oral cleft in neonates exposed to corticosteroids in the first trimester.

Antibiotics: Metronidazole (FDA Class B) and Ciprofloxacin (FDA Class C) are commonly used to treat abscesses and fistulae in IBD. Animal studies showed carcinogenic effects from Metronidazole, and early studies suggested a risk of cleft lip[55], but this has not been reported in humans[71]. It was not associated with preterm birth (OR = 1.02, 95%CI: 0.80-1.32), low birth weight (OR = 1.05, 95%CI: 0.77-1.43), OR = congenital anomalies (OR = 0.86, 95%CI: 0.30-2.45) in a large study of 2829 singleton/mother pairs[72]. In a small study (27 of 113 patients on Metronidazole) in female IBD patients, metronidazole was found to be safe in all trimesters of pregnancy[49]. Previously, there was concern that quinolones increase the risk of arthropathies in the offspring, Studies have reported no significant increase in major congenital anomalies, including musculoskeletal problems from the use of ciprofloxacin[73]. A meta-analysis of pregnancy outcomes after exposure to quinolones in the first trimester reported no increased risk of major malformations, stillbirths, preterm births, or low birth weight[74]. However, because of the known possible effect of ciprofloxacin on bone and cartilage, it has been recommended to avoid this medication during pregnancy[55].

Penicillins have not been shown to cause fetal malformations or adverse pregnancy outcomes, and are considered the first line therapy in pregnancy[71]. Amoxicillin (FDA Class B) can be used to treat abscesses and complications of IBD during pregnancy.

Action point: Metronidazole can be used during pregnancy, preferably avoid use in first trimester. Ciprofloxacion should be avoided during pregnancy due to risk of arthropathy. Amoxicilin is safe to use during pregnancy.

Biologics: Anti-tumour necrosis factor inhibitors (FDA Class B) such as Infliximab, Adalimumab, and Certolizumab, are commonly used to treat moderate to severe IBD, and fistulizing Crohn's disease. TNF-α is a pro-inflammatory cytokine that stimulates the production of prostaglandins, and increased levels are associated with preterm labor[75]. TNF levels increase during pregnancy, as it is mainly produced by the placenta[76]. TNF-α is important for the initial stages of pregnancy, and also for the development of the fetal immune system, and TNF deficient animals have been shown to have increased risk of immune developmental abnormalities[77]. However, increased levels of TNF-α have been associated with preeclampsia, gestational diabetes, obesity[76].

Initially Infliximab and Adalimumab were reported in a few cases of pregnant women with IBD[78-84] which did not show any adverse effects. Larger observational studies, registry studies, and systematic reviews have shown its safety for use during pregnancy[85-88]. The PIANO study has not found any increase in congenital anomalies, abnormal newborn growth and development, or other complications, among women receiving biologics[62].

Infliximab and Adalimumab are IgG1 monoclonal antibodies, and are actively transported across the placenta, while Certolizumab is a Fab fragment of IgG1, and has not been shown to have placental transportation[89]. This active transport of IgG1 antibodies occurs mainly in the third trimester[81,90]. Thus it has been recommended to stop Infliximab and Adalimumab at the onset of the third trimester[91,92]. However, in a recent study, in women with quiescent IBD, who discontinued anti-TNF therapy by week 30, Infliximab and Adalimumab were still detected in cord blood[93]. The exact time to hold anti-TNF is now debatable, especially with Adalimumab which is given weekly or biweekly, but in high risk patients, or patients with active disease, these biologics should be continued throughout the pregnancy[94]. Levels of Infliximab and Adalimumab have been detected in infants for as long as 6 mo[95]. At least for the short term, children exposed to intra-uterine Infliximab develop normally, without increased infections, allergic reactions, or decreased response to vaccinations[91]. However, infants exposed to combination of immunomodulators and biologics have been noted to have increase in infections from 9 to 12 mo of age[62]. Thus, it is still recommended that infants exposed to intra-uterine anti-TNF therapy delay live vaccinations for at least the first 6 mo.

Action point: Anti-TNF therapies are safe to use during pregnancy. Infliximab and Adalimumab should be held after week 30, if not earlier, to decrease placental transport to the fetus. Neonates exposed to biologics during pregnancy should not have live vaccines during the first 6 mo post delivery.

Cyclosporine (FDA Class C): Cyclosporine crosses the placenta, and has not been found to be teratogenic in animal models[96]. The majority of studies on cyclosporine in pregnancy involve post-transplant patients, which suggests an association with premature delivery and low birth weight infants[97]. In severe ulcerative colitis flares during pregnancy, cyclosporine has been used with successful control of the disease, avoidance of colectomy during pregnancy, and no significant adverse pregnancy outcome[98-104]. The most common side effect reported was hypertrichosis in the mother, however, in one case report, the patient developed severe hypertension and seizures 48 h post infusion[99]. Other adverse effects of cyclosporine include nephrotoxicity and hepatotoxicity[97].

Fulminant ulcerative colitis leading to colectomy has been associated with adverse pregnancy outcomes, with up to 49% fetal mortality and 22% maternal mortality rates in the literature[105]. Thus, in cases of severe fulminant ulcerative colitis, in order to avoid urgent colectomy, cyclosporine may be considered.

Action point: Cyclosporine may be considered in cases of severe fulminant ulcerative colitis in pregnancy, in order to avoid colectomy during pregnancy. However, as biologics are FDA Class B, and there are more studies on Infliximab use during pregnancy, Infliximab may be the preferred first line option.

Managing relapses during pregnancy: can we use induction medications?

As already mentioned, active disease during pregnancy is associated with poor pregnancy outcomes. Since medications commonly used to treat IBD are not associated with significant adverse pregnancy outcomes, treating the mother to induce and maintain remission during the remainder of the pregnancy will lead to more beneficial outcomes. If hospitalization is required to manage an acute IBD flare, IV hydrocortisone[103] and IV infliximab[78,82,91,92,106] may be used for rescue therapy, as thus far, they have not been associated with significant adverse effects. One study has shown that IV cyclosporine can be used safely[103].

Action point: Active IBD is associated with adverse pregnancy outcomes. Management of flares of IBD during pregnancy may involve the use of steroids, biologics, and possibly cyclosporine.

DELIVERY

Women with IBD were initially reported to be more likely to have a caesarean section[2,14,25,33,34,107]. This has mainly been attributed to Crohn's disease patients, especially those with perianal disease[14,107,108]; it has also been shown that vaginal delivery with episiotomy may be associated with subsequent perianal involvement[109]. Larger population studies found no significant difference in caesarean section rates among IBD patients[38], and no risk of progression of perianal disease in Crohn's disease with vaginal delivery[108]. Thus, the decision for caesarean section should not be made purely on the IBD diagnosis, but also obstetrical reasons.

Action point: In women with Crohn's disease with active perianal disease, caesarean section should be considered on an individual basis.

POST PARTUM

What is the risk of IBD flaring after delivery?

Some women may flare after delivery, while others fare well. A retrospective cohort study of 114 Crohn's disease patients reported more frequent disease progression after childbirth in patients who had active luminal disease prior to pregnancy[108]. A large multi-country prospective study found higher risk of relapse in the postpartum period in women with ulcerative colitis[43].

Action point: Ulcerative colitis patients have an increased risk of relapse after delivery. Crohn's disease patients with active luminal disease before pregnancy have a higher risk of relapse after delivery.

BREASTFEEDING

Breastfeeding physiologically may be associated with increased inflammation, as prolactin is associated with up-regulation of TNF production[110] and increased levels are found in other autoimmune diseases such as lupus, rheumatoid arthritis[111]. Many women with IBD choose not to breastfeed their children[2,112]. This may be due to fears of medication effects, physician recommendation or personal choice[112]. The effect of breastfeeding on the development of IBD is thought to be related to the hygiene hypothesis, in which breastfeeding is thought to help the neonate develop tolerance to microflora and food antigens, thus preventing immune over activation to delayed antigen exposures[113-115].

Does breastfeeding affect IBD?

Studies investigating the effect of breastfeeding on developing IBD vary in methodology and conclusions. In one study, women who breastfeed were found to be more likely to have a postpartum flare of their disease, but this increased risk was non significant once adjusted for discontinuation of IBD medications during pregnancy[112]. A more recent population-based study found no increased rate of disease flare in the post partum year between those who breastfed (26%) *vs* those who did not (29.4%)[116].

Can breastfeeding affect the risk of IBD in the offspring?

Some studies find no association between breast feeding and diagnosis of IBD[117]. However, some report that a lack of breastfeeding in infancy is associated with an increased risk of UC (OR = 1.5, 95%CI: 1.1-2.1) and

CD (OR = 1.9, 95%CI: 1.1-3.3)[118]. More recent studies reported a protective effect of breastfeeding to decrease the odds of developing IBD[119,120]. Two systematic reviews investigating the role of breastfeeding and the development of IBD found that breastfeeding is associated with lower risks of developing early-onset IBD[121,122].

Which medications can be used during breastfeeding?

Aminosalicylates (FDA Class B, Asacol FDA Class C) and sulfasalazine (FDA Class B): Earlier studies have reported the rare occasion of infants exposed to 5-aminosalicylates via breast-milk developing watery diarrhea[123], however very small amounts of drug are excreted into breast milk, making risk of toxicity and reaction very unlikely[124-126]. Sulphasalazine has also been reported to cause bloody diarrhea in the infant exposed via breast-milk[127], however, it has not been reported other than case reports. Sulfasalazine can have a bilirubin displacing effect leading to jaundice in the neonate, however the amount of drug transferred to the child via breast-milk is negligible to cause jaundice[128,129].

ACTION POINT: 5-aminosalicylates and sulphasalazine can be continued during breastfeeding.

Azathioprine and 6-mercaptopurine/Purinethol (FDA Class D): Azathioprine and 6-MP can be continued during pregnancy, as described above, but there are concerns about the potential for tumorigenicity, and increased susceptibility to infections in neonates exposed during breastfeeding[66]. Recent studies show that only very small amounts of AZA/6-MP are measured in breast milk, and neglible amounts detected in the neonate[130-134]. In addition, the highest concentration of AZA measured in the breast milk appears during the first 4 h after consumption[130], thus it has been recommended to "pump and dump" the first 4 h of breastmilk. Thus far, there has not been reported increase risk of infections among babies breastfed with exposure to azathioprine[66], and it is considered safe to continue these medications during breastfeeding[54,66,130-134].

Action point: Azathioprine and 6-MP are can be continued during breastfeeding; the first 4 h of breastmilk after consumption may be discarded to minimize the amount of drug transferred to the neonate.

Methotrexate (FDA Class X): Methotrexate crosses into the breast milk[135] and because of its teratogenicity, it is contraindicated during breastfeeding[136,137].

Action point: Methotrexate is contraindicated during breastfeeding.

Corticosteroids (FDA Class C): Corticosteroids do transfer to the breast milk, but in very low levels[138,139] and because the highest levels appear in the first 4 h[139], it is recommended to "pump and dump"[55,139] the first 4 h after medication consumption to minimize transfer of the drug to the neonate.

Action point: Corticosteroids can be continued during breastfeeding if required to treat maternal IBD.

Antibiotics: Metronidazole is transferred into the breast milk[139], but in minimal levels[140] and levels decline after 12-24 h after maternal dose intake[141]. If metronidazole is required for the treatment of active IBD, it is recommended to wait 12-24 h after metronidazole intake before breastfeeding[55], and long term use should be avoided[69]. Ciprofloxacin is also detectable in the breast milk in small amounts[142,143], but short term treatment can be used if indicated[55].

Action point: Metronidazole and ciprofloxacin can be continued for short term during breastfeeding if required to treat maternal IBD.

Biologics: As mentioned, the biologic therapies can be continued during pregnancy, and held in the third trimester. Studies have shown nil to minimal levels of infliximab and adalimumab in the breast milk and no significant adverse events have been reported in the infant[81,143-148]. It is thought that any detectable levels in the neonate after delivery may be due to placental transfer during pregnancy[147]. Thus, although anti-TNF therapies are can be continued during breastfeeding, further studies are required to determine the effect of infant exposure to these biological therapies on the development of their gastrointestinal immunity and systemic immune system[89,146,148]. The preliminary results of the PIANO study have not found any association between breastfeeding and infection risk in the neonate exposed to biologic therapy[62].

Action point: Infliximab and adalimumab may be continued during breastfeeding.

Cyclosporine (FDA Class C): Cyclosporine does cross into the breast milk, but if required for fulminant colitis, it can be used. Case reports and series of neonates exposed to cyclosporine during pregnancy and breastfeeding are mainly from the renal transplant literature, and have reported varying levels of cyclosporine in the breast milk, and relatively good outcomes in the mother and neonate[149-153]. One case report of cyclosporine use in the management of severe ulcerative colitis while breastfeeding also reported short term good outcomes in the mother and neonate[154]. More studies are required to determine the long term effects of neonatal exposure to cyclosporine in the breast milk.

Action point: Cyclosporine has been used to manage fulminant colitis during breastfeeding, however, infliximab is preferred due to the lack of studies for cyclosporine.

CONCLUSION

IBD affects people during an important time of their lives when they are considering family planning or are already pregnant. With the exception of Methotrexate, commonly used medications for the treatment of IBD are not associated with significant adverse pregnancy outcomes, and can be used throughout pregnancy. Good control of disease and clinical remission at the time of conception increases the likelihood of having successful pregnancy outcomes, and quiescent disease during pregnancy. There is no need to adjust medications during pregnancy, with the exception of biologics such as Infliximab and Adalimumab, which should be held during the third trimester in women who are in clinical remission. However, biologics may be continued throughout pregnancy if necessary to control disease. Induction of remission of IBD flares during pregnancy should be treated with appropriate medications, such as steroids, infliximab, and for severe fulminant colitis, cyclosporine, as active disease and fulminant colitis requiring surgery has increased risk of adverse fetal outcomes. The management of IBD in women during their reproductive years should include consideration of their family planning decisions, and education counseling regarding the overall safety of medications and the importance of medication adherence should occur prior to conception.

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