PSC and Inflammatory Bowel Disease (IBD): Women’s Health Issues

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Presentation Overview

- Gynecologic issues and family planning
- Effect of pregnancy on IBD and PSC
- Effect of IBD and PSC on pregnancy
- Treatment in pregnancy
- Delivery
- Breastfeeding
- Vaccines
Meet Heather... 

- 17 y.o. female recently diagnosed with extensive ulcerative colitis (UC) and PSC
- She is started on prednisone and mesalamine
- Difficulty tapering off of prednisone so started on azathioprine and responds well
- She is not sexually active
- She has questions about birth control
Contraception is Safe in PSC with IBD

Choices for Contraception are Generally Same as those for General Population

- Hormonal or non-hormonal **intrauterine device** or contraceptive implants are safest/most effective

- Non-estrogen containing contraception is preferred due to increased risk of venous thromboembolism
  - Low-dose estrogen OCP is okay if no other risk factors for thromboembolism

- Active small bowel IBD or extensive small bowel resection can affect absorption and efficacy of oral contraceptives

- Cirrhosis: no restriction, except in severe decompensated cirrhosis (lack of data)
Heather... 

1 year later develops severe flare and hospitalized

Unresponsive to IV steroids and started on infliximab

Responds well and continues on azathioprine and mesalamine as well
Heather...  

- 2 years later she is having recurrent symptoms  
- Planning on getting married next year to Steve  
- Wants to have children in the future  
- Worries about future surgery if symptoms persist as her sister underwent IPAA for medical refractory UC and had trouble conceiving after
Fertility in PSC with IBD

- **Fertility**: achieving pregnancy within 1 year of intercourse without contraception
  - Background rate – 1 in 7 couples (14%)
- Majority of women with IBD or PSC have normal fertility
- Potential impact on infertility
  - Disease activity in IBD
  - Decompensated PSC cirrhosis (no menstrual cycles)
  - Medication (sulfasalazine in men)
  - Voluntary
  - Surgery
Heather... 

- Medications adjusted and she has been in remission for 2 years

- Actively trying to conceive

- Wonders about risk of her baby developing IBD
Heritability of IBD and PSC

- Inheritance is major concern expressed by patients considering having children
- **IBD**: family history is most important risk factor to predict lifetime risk
- CD is more often familial than UC
- Children of CD parent have 5-10% lifetime risk of IBD (2% with UC)
- 2 parents affected (1 with CD) have 35% lifetime risk
- **PSC**: genetic risk variants identified, but familial disease is rare; there is no genetic testing available
Heather and Steve...

- She is now 2 months pregnant and has an appointment with MFM

- She wonders how her disease will affect her baby and likewise how being pregnant could affect her colitis and PSC
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Effect of Pregnancy on IBD
Effect of Pregnancy on CD Disease Activity at Conception

Effect of Pregnancy on UC
Disease Activity at Conception

Effect of Pregnancy on PSC
Pregnancy Does Not Worsen PSC Progression, But Can Complicate Cirrhosis

- **PSC**
  - Portal hypertension
  - NO CIRRHOSIS
  - Portal hypertension

- **CIRRHOSIS**
  - Complications in 30-50% of patients
  - EGD to screen for esophageal varices prior to conception and 2nd trimester
  - Treat varices to prevent bleeding
  - Ultrasound to screen for splenic artery aneurysm
  - Risk of complications: ascites (10%), variceal bleeding (7%), encephalopathy (1%)

- **NO CIRRHOSIS**
  - Itching may occur
  - Consider UDCA

Pregnancy can be completed safely under close medical supervision
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Guiding Principle in Pregnant Patients with Active IBD

“The greatest risk to pregnancy is active disease—not active medicine.”

Goals
- Establish remission before conception
- Maintain remission during pregnancy

Basic science studies suggest that active inflammation bad for any pregnancy, not just in IBD

Effect of IBD on Pregnancy Outcomes

- Case-controlled studies and population based studies suggest:
  - Increased risk of adverse pregnancy outcomes
  - Spontaneous abortion
  - Low birth weight
  - Preterm delivery
  - Complications of L&D (pre-eclampsia, liver, and platelet disorders)
  - C-section rate
  - No major impact congenital abnormalities

- Likely influenced by disease activity
Impact of PSC Cirrhosis on Pregnancy

- **Maternal risk:**
  - correlates with liver disease severity. MELD \( \geq 10 \) has worse outcomes

- **Fetal risk:**
  - higher rate of prematurity and early fetal loss (20% vs 3-6% in general population)
  - Lower live birth rate (58%)
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# Safety of IBD Medications During Pregnancy

<table>
<thead>
<tr>
<th>Safe to Use When Indicated</th>
<th>Limited Data Available</th>
<th>Contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral mesalamine</td>
<td>Cyclosporine</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Topical mesalamine</td>
<td>Natalizumab</td>
<td>Thalidomide</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>Vedolizumab</td>
<td>Rifaximin</td>
</tr>
<tr>
<td>Metronidazole/Cipro?</td>
<td>Ustekinumab</td>
<td></td>
</tr>
<tr>
<td>Anti-TNF agents</td>
<td>Tofacitinib (likely contraindicated)</td>
<td></td>
</tr>
<tr>
<td>Azathioprine/6-MP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
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</tbody>
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Placental Transfer of Biologics

- Infliximab and adalimumab do not cross the placenta in the 1\textsuperscript{st} TM
  - 1\textsuperscript{st} TM important for organ/neural development
- Cross efficiently in the 3\textsuperscript{rd} TM
- Infliximab is detected in infant blood up to 6 months from birth
- Certolizumab is pegylated Fab portion of Ab
  - Minimal placental transfer by passive diffusion
Newer Biologics

- **Vedolizumab**
  - Low risk; limited data

- **Ustekinumab**
  - Low risk; limited data

- **Tofacitinib**
  - Limited data, teratogenic in animal studies
  - Not recommended in pregnancy

Mahadevan et al. Gastroenterology 2017
Moens et al. J Crohns Colitis 2019
Heather...

- 28 weeks pregnant, on bedrest for pre-term labor
- No colitis symptoms
- Wonders about infliximab dosing
- She is due for dose in 2 weeks
- Ob feels she will likely deliver early 36wks?
- When should she get her last infliximab dose?
Minimizing Placental Transfer

Adjustment of dosing schedule

<table>
<thead>
<tr>
<th>Biologic</th>
<th>Timing of Last Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>Week 30-32</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Week 36-37</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Golimumab</td>
<td>Week 34-36</td>
</tr>
<tr>
<td>Natalizumab</td>
<td>Week 34-36</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>Week 30-32</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>Week 30-32</td>
</tr>
</tbody>
</table>

Resume biologic:
- 24 hours after vaginal delivery
- 48 hours after c-section
Pregnancy After Liver Transplant (LT)

- **Impact of LT on fetus**
- Early conception within 12 months after LT is a risk factor for stillbirth → **WAIT 1 year after LT**
- Live birth: 69-77% of pregnancies
- Higher rate of complications: preeclampsia (22%), cesarean section (45-50%), and premature delivery (31-39%)
- Antirejection medications can lead to congenital malformations and miscarriage → **DISCONTINUE**:
  - mycophenolate mofetil
  - sirolimus
Pregnancy After Liver Transplant (LT)

- Impact of pregnancy on the liver allograft
  - Pregnancy increases the risk of rejection
  - The risk is higher with early pregnancy vs 1 year after LT: 46% compared with 11%

Avoid unplanned pregnancy in the first year after LT!
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Mode of Delivery

- Women with IBD or cirrhosis have 1.5-2-fold greater risk of C-section
  - Women with UC and perianal CD have increased risk of C-section
- Delivery method should be at discretion of OB/Mom
- Most women with IBD can have vaginal delivery
- Exceptions: those who need C-section:
  - Active (or quite recent) perianal disease
  - History of rectovaginal fistula
  - UC patients with J pouch (?)
  - Women with large esophageal varices

Burke KE et al. Inflamm Bowel Dis 2017
Manosa et al. Scand J Gastroenterol 2013
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Breastfeeding: IBD Medications

- **LactMed**
  - US National Library of Medicine
  - free online database

- Most IBD medications are safe for breastfeeding
# Summary: IBD Meds & Breastfeeding

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommendation</th>
<th>Potential concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminosalicylates</td>
<td>Compatible</td>
<td>Rare diarrhea in infant</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Probably compatible</td>
<td>Delay feeding 4 hours</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>Compatible</td>
<td></td>
</tr>
<tr>
<td>Rifaximin</td>
<td>Avoid</td>
<td>No human data</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Compatible</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td>Thiopurines</td>
<td>Compatible</td>
<td>Delay feeding 4 hours</td>
</tr>
<tr>
<td>Biologics</td>
<td>Compatible</td>
<td>Low or undetectable levels (Vedo unknown)</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Post-Liver Transplant Meds & Breastfeeding

- Compatible: tacrolimus, cyclosporine, prednisone, UDCA

- Limited data: sirolimus, MMF
Take Home Points

- Majority of women with IBD and non-cirrhotic PSC have normal fertility
- Contraception is safe in PSC with IBD
- The greatest risk to pregnancy is active disease—not active medicine
- Pregnancy is contraindicated in cirrhosis with MELD>10 or portal hypertension (varices, ascites)
- Pregnancy after transplant has good outcomes if conception occurs >1 year after LT
- Most medications can be continued during pregnancy and lactation
- Interdisciplinary approach is essential
Questions & Discussion