Pregnancy & Fertility in IBD

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Agenda & Learning Objectives

• Be able to define fertility, fecundity, and infertility

• Recognize ways to prepare and plan ahead for successful pregnancy in Inflammatory Bowel Diseases

• Identify steps that can be taken to optimize the health of both mother and child during pregnancy

• Understand concerns surrounding post-delivery care in the setting of Inflammatory Bowel Diseases

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Why Plan Ahead for Pregnancy in IBD?

- Women with IBD typically have normal pregnancies and healthy infants compared to women without IBD.
  - Also more likely to have higher rates of pregnancy complications including:
    - Premature delivery/preterm births
    - Low birth weight
    - SGA
  - Active IBD associated with miscarriage and stillbirth

- Thus all women with IBD should be followed as high-risk obstetric patients.
- Pregnancy planning allows medical optimization to improve chances of successful outcomes for both the pregnancy and IBD.
## Pregnancy outcomes: Population-based studies

<table>
<thead>
<tr>
<th></th>
<th>IBD</th>
<th>UC</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm birth</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Smallness for gestational age</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Congenital malformation</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Cesarean section</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Kornfeld: *Am J Obstet Gynecol* 1997 (n=756 IBD)  
Fonager: *Am J Gastroenterol* 1998 (n=510 CD)  
Nørgård: *Am J Gastroenterol* 2000 (n=1531 UC)  
Dominitz: *Am J Gastroenterol* 2002 (n=107 UC, 155 CD)  

Pregnancy outcomes in a US population

- Retrospective cohort study
- n=461 IBD, 493 controls
- 5-ASA (51%), corticosteroids (21%), immunosuppressants (4%)

<table>
<thead>
<tr>
<th>Adverse outcomes</th>
<th>OR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conception</td>
<td>1.65</td>
<td>1.09–2.48</td>
</tr>
<tr>
<td>Pregnancy outcomes</td>
<td>1.54</td>
<td>1.00–2.38</td>
</tr>
<tr>
<td>Pregnancy complications</td>
<td>1.78</td>
<td>1.13–2.81</td>
</tr>
<tr>
<td>Newborn outcomes</td>
<td>1.89</td>
<td>0.98–3.69</td>
</tr>
</tbody>
</table>

*Controlled for maternal age, current ETOH, current tobacco, Caucasian ethnicity, number of prenatal visits (except conception)

*Mahadevan et al, Gastroenterology 2007; 133: 1106–12*
Definitions

- **Fecundity:**
  - The ability to have children
  - Fecundation = fertilization (natural or IVF)

- **Fertility:**
  - The ability to conceive and become pregnant through normal sexual activity

- **Infertility:**
  - Failure to conceive after 1 year of intercourse
  - Background rate: 1 in 7 couples (14%)
**Fertility**

- With both UC and CD, the risk of infertility prior to surgery appears similar to the general population
  - Infertility in NE Scotland population-based study\(^1\)
    - 15% UC (n=138) vs 14% general population
    - 14% CD (n=177) vs 14% general population
      - Surgical therapy 20%; medical therapy 8%

- Significant reduction in fecundability with IPAA surgery first shown in Ording Olsen study of 290 women with UC with ileal pouch anal anastomosis (IPAA)\(^2\)
  - Fecundability after diagnosis of UC: FR = 1.01
  - Fecundability after surgery for IPAA: FR = 0.20 (p<0.0001)

\(^1\) Hudsen et al. *Int J Gynaecol Obstet* 1997;58:229-37
\(^2\) Ording Olsen et al. *Gastroenterology* 2002;122:15-9
Risk of infertility in UC increases threefold after ileal pouch-anal anastomosis (IPAA)*

Study | Relative Risk (95% CI) | % Weight |
--- | --- | --- |
Wikland | 1.93 (0.92, 4.03) | 9.9 |
Oresland | 14.40 (0.98, 211.94) | 1.2 |
Counihan | 3.60 (1.39, 9.35) | 9.1 |
Sjogren | 1.00 (0.32, 3.10) | 9.1 |
Hudson | 3.38 (1.66, 6.89) | 5.8 |
Olsen | 3.62 (2.42, 5.41) | 44.1 |
Johnson | 2.89 (1.47, 5.68) | 20.9 |

Overall (95% CI) | 3.17 (2.41, 4.18) |

*Compared to medical management

Conception and IBD

- Women with IBD in remission can generally conceive and become pregnant as easily as women of the same age without IBD.

- However, women with active disease (not in remission) may have more difficulty becoming pregnant.

- Pelvic surgeries (e.g., colectomy with ileoanal J-pouch) may further reduce fertility rates.

- If a couple is having difficulty conceiving despite trying for 6 months, consider seeing a fertility specialist.
Effect of Pregnancy on IBD

- In general, women with IBD have the same risk of flares during pregnancy as they do when they are not pregnant.

- IBD activity may even be slightly lower as a result of pregnancy, with reduced relapse rates reported even 10 years following pregnancy (both UC and CD).
Effect of IBD on Pregnancy

The disease activity of the IBD at the time of conception helps to predict adverse outcomes in pregnancy.

- Active IBD at the time of conception is associated with increased fetal loss (abortion, stillbirth) and preterm births.
- Active IBD during pregnancy is associated with low birth weight and preterm births.

Therefore, women with IBD should be counseled to try to conceive when in remission.

- Patients who are in clinical remission (inactive IBD) at time of conception are more likely to remain inactive, without relapses of their IBD, during pregnancy.
Effect of Pregnancy on IBD: Disease Activity at Conception

Miller JP. J R Soc Med 1986;79:221-225
Disease activity during pregnancy in women with IBD

- Exposure: IBD activity during conception, each trimester and the postpartum period (1 month)

**Patients (%)**

**Disease activity in Crohn’s disease**

- Inactive
- Mild
- Moderate
- Severe

**Disease activity in ulcerative colitis**

- Inactive
- Mild
- Moderate
- Severe

Mahadevan et al, Gastroenterology 2007; 133: 1106–12
Inheritance: What Are the Chances My Child Will Have IBD?

- Increased risk of CD and UC in offspring of patients with IBD than the general population, although it is not inevitable that they will develop IBD
  - If 1 parent has IBD, the chance of a child developing the condition is ~ 2-9% (5% if CD, 1.6% if UC)
  - If both parents have IBD, the child's risk for developing IBD is as high as 36%
  - Familial CD has earlier onset than sporadic cases (average age 22 yrs vs 27 yrs, respectively)

- Inheritance is multifactorial with a role for as yet undefined environmental triggers

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1 Orholm et al. *Am J Gastroenterol* 1999;94:3236-8
2 Bennett et al. *Gastroenterology* 1991;100:1638-43
1. Before Pregnancy…
Build a Cohesive Medical Team

- Develop a therapeutic alliance with a multidisciplinary team, including:
  - High risk (+general) obstetrician
  - Gastroenterologist/ IBD specialist
  - Pediatrician
  - General practitioner
  - Colorectal surgeon
  - Social worker
  - Nutritionist
  - Counselor
  - Psychologist/Psychiatrist
Baseline IBD Assessment

- Prior to conception, consider initial assessment of baseline disease activity and severity via laboratory and endoscopic evaluations (i.e., colonoscopy with biopsies)

- This can be used to stratify the patient’s risk for active disease during pregnancy and to help predict the outcomes of pregnancy
Review Medications

- Encourage honest and open discussion to review medication safety profiles, explore medical options and alternatives, and clarify patient preferences and goals of care

- Certain medications (including methotrexate, thalidomide) should be discontinued several months in advance of planned conception, as they pose risks to a developing fetus

- The majority of other medications used in IBD may be continued throughout pregnancy
Nutritional Support

- Encourage a well-balanced diet

- Recommend prenatal vitamins and folic acid 1 mg twice a day (for a total of 2 mg daily)
  - Folic acid deficiencies: neural tube defects including spina bifida, cardiovascular, genitourinary, cleft palate
  - Note: higher than 1mg daily dose recommended for general population because IBD patients may have folic acid deficiencies or take medications that interfere with folic acid metabolism (e.g., sulfasalazine)

- If on corticosteroids, should encourage calcium and vitamin D supplementation to prevent bone loss
Keep Routine Healthcare Maintenance Up to Date

- Vaccinations
- Pap smears
- Vitamin levels
- Colon cancer surveillance
Alcohol & Tobacco Cessation

- Alcohol consumption during pregnancy can result in mental, learning, and behavioral disabilities or Fetal Alcohol Spectrum Disorders (FASDs) or fetal alcohol syndrome (FAS).
  - FAS is a permanent birth defect characterized by growth deficiency, CNS damage/dysfunction, and facial abnormalities.

- Tobacco use during pregnancy associated with preterm birth, placenta previa, placental abruption, premature rupture of membranes, intrauterine growth restriction, sudden infant death syndrome (SIDS).
2. During Pregnancy…
Medications

- Maintaining the mother’s health remains a top priority in the management of pregnant IBD patients
  - In general, most medications are maintained consistently throughout pregnancy, unless the mother’s condition changes
- Avoid methotrexate, thalidomide, and certain antibiotics
- The majority of other meds for inducing/maintaining remission are considered low risk, and may be continued after discussion with the patient
  - The risk of developing an adverse event with a medication must be weighed against the potential benefit to the mother’s health if she were to continue on the medication
- Once treatment plan agreed upon, patients should be counseled on strict adherence to minimize the risk of flares during pregnancy

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# Medical therapy: FDA pregnancy category

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Controlled studies show no risk</td>
</tr>
<tr>
<td>B</td>
<td>No evidence of risk in humans</td>
</tr>
</tbody>
</table>
| C        | - Animal reproduction studies show adverse effects  
               - No adequate studies in humans  
               - Benefits in pregnant women may be acceptable despite potential risk |
| D        | Positive evidence of risk |
| X        | Contraindicated in pregnancy |
### Medical Therapy: FDA Pregnancy Category

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pregnancy Category</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminosalicylates</td>
<td>B, except C for olsalazine</td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Rifaxamin</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Augmentin</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Azathioprine/6-Mercaptopurine</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>Infliximab</td>
<td>B</td>
<td>Stop week 30</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>B</td>
<td>Stop week 30-34</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>B</td>
<td>Continue throughout</td>
</tr>
<tr>
<td>Drug</td>
<td>Pregnancy category</td>
<td>Notes</td>
</tr>
<tr>
<td>--------------------</td>
<td>--------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>Diphenoxylate</td>
<td>C</td>
<td>Teratogenic in animals</td>
</tr>
<tr>
<td>Loperamide</td>
<td>B</td>
<td>Increase in CV defects in 1 study</td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>C</td>
<td>■ Animal studies: Alendronate crosses placenta</td>
</tr>
<tr>
<td></td>
<td></td>
<td>■ 24 pregnancies, no increased teratogenic risk(^1)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>X</td>
<td>■ Known abortifacent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>■ Teratogenic (skeletal defects; cleft palate)</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>X</td>
<td>■ Birth defects</td>
</tr>
</tbody>
</table>

\(^1\)Ornoy et al, Reprod Toxicol 2006; 22: 578–9
Mode of Delivery

- Typically left to the high-risk obstetrician’s discretion
  - Most women with IBD can have uncomplicated vaginal delivery

- Exceptions:
  - Active perianal IBD (fistulas, abscess) should have C-section
    - Women with inactive perianal disease may deliver vaginally without increased complications\(^1\)

- Some patients with ileoanal J-pouch should consider C-section, although vaginal delivery is possible\(^2\)
  - May preserve anal sphincter function and continence later in life

\(^1\)Ilnyckyji et al. *Am J Gastroenterol* 1999;94:3274-8
\(^2\)Juhasz et al. *Dis Colon Rectum* 1995;38:159-65
IBD Assessments During Pregnancy

- Can be performed safely during pregnancy:
  - Colonoscopy or unsedated flexible sigmoidoscopy with biopsies
  - EGD
  - Abdominal ultrasound

- Avoid when possible:
  - Standard X-rays or CT scans
  - MRI with gadolinium in first trimester (renal damage)
Surgery During Pregnancy

- Indications similar to non-pregnant patient

- Postpone until after delivery whenever possible, as abdominal surgeries pose risks to the fetus, but 2\textsuperscript{nd} trimester is best time to operate if needed
Nutritional Support During Pregnancy

Continue to encourage well-balanced diet and vitamin supplementation, including folic acid, as before pregnancy.
3. After Delivery
Breastfeeding and Lactation

- Actively encourage breastfeeding when possible
  - Only a small percentage of IBD patients breastfeed their children, due to fear of medication compatibility with breastfeeding
  - Avoid breastfeeding in patients on methotrexate, thalidomide, cyclosporine, tacrolimus, and metronidazole
  - Dose 6MP/AZA 4 hours prior to feeding (as majority in breast milk within 4 hours of drug intake)
  - Risks of breastfeeding while taking medications potentially harmful to the newborn must be weighed against the benefits of breastfeeding and therapy

- Nursing mothers should use caution when taking fenugreek, an herbal supplement commonly used to increase lactation) → increased risk of rectal bleeding in IBD
Compatible with Use in Lactation

- 5-ASA
- Corticosteroids
- Antibiotics except metronidazole
- Azathioprine/6-mercaptopurine—but dose this 4 hours prior to feeding
- Infliximab
- Adalimumab
- Certolizumab
Infant Vaccinations

- Mothers who took immunosuppressive medications while pregnant should be informed that their infants should not receive any live vaccinations during the first 6 months of life (including rotavirus vaccine).

- All non-live vaccines may be administered on schedule.

- Mothers on immunosuppressive medications should use caution in handling the body fluids of infants who recently received a live virus vaccination.
Thank You
Contact Info for the UCLA Center for IBD

- 2 convenient locations:
  - Westwood (200 Medical Plaza, Ste 365-C, Los Angeles, CA 90095)
  - Santa Monica (1223 16th St, Ste 3100, Santa Monica, CA 90404)

- Email: ibdcenter@mednet.ucla.edu
- Phone: (855) IBD-UCLA / (855) 423-8252
- Fax: (310) 206-9906

- Website: www.uclaibd.com
- Facebook: https://www.facebook.com/UCLAIBD (Like us!)
- Twitter: https://twitter.com/UCLAibd (Follow us!)
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