

Achieve IBD Remission Before Pregnancy: PIANO Registry Data Shows Adverse Perinatal Outcomes For Infants Associated with IBD Flares and Steroid Use



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This summary reviews: Odufalu FD, Long MD, Lin K, Mahadaven U for PIANO Investigators. Exposure to Corticosteroids in Pregnancy Is Associated with Adverse Perinatal Outcomes Among Infants of Mothers with Inflammatory Bowel Disease. *Gut* 2022; 71: 1766-72.

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STRUCTURED ABSTRACT

Question: Is corticosteroid use in inflammatory bowel disease (IBD) patients during pregnancy associated with increased adverse maternal and fetal outcomes?

Design: A prospective, multicenter, observational cohort study.

Setting: Thirty centers in the United States.

Patients: The study enrolled 1,712 pregnant women with IBD between 2009 and 2019, representing 1,490 completed pregnancies, 1,431 live births, and 1,010 infants with one-year developmental measurements available.

Exposures: Corticosteroid use by oral, enema, or IV routes of administration stratified by 4 points in time: preconception, first trimester, second trimester, and third trimester. Study patients completed detailed questionnaires at study entry, each trimester, and 4, 9, and 12 months after birth. Questionnaires pro-

vided demographic data, IBD history, IBD activity, medication exposure, pregnancy outcomes, postpartum outcomes and complications. IBD activity was measured with modified Harvey Bradshaw Index for Crohn's Disease (CD) and the simple clinical colitis activity index (SCCAI) for ulcerative colitis (UC)

Outcome: Primary outcomes were infant outcomes, including adverse pregnancy-related events, congenital malformations, infections, and neurocognitive development during the first 12 months. Secondary outcomes were maternal outcomes of delivery complications, preterm labor, caesarean sections, and trends in IBD activity.

Data Analysis: Bivariate statistics and multivariate logistic regression models were used to compare pregnancy outcomes by corticosteroid exposure. Odds ratios were adjusted for relevant confounders, including preterm birth, maternal disease activity, and classes of medication use.

Funding: The study was funded by the Crohn's & Colitis Foundation, Lisa and Douglas Goldman Foundation, Lab and Valibhav Goel Foundation, and the National Institutes of Health.

Results: Corticosteroid use was associated with preterm birth (odds ratio [OR]= 1.79; 95% confidence interval [CI]: 1.18-2.73); low birth weight (OR= 1.76; 95% CI: 1.07-2.88), and NICU admission (OR= 1.54; 95% CI: 1.03-2.30). (**Table 1**) Late corticosteroid use (second and/or third trimester) was associated with serious infant infections at 9 months (4% vs 2%, $P= 0.03$) and 12 months (5% vs 2%, $P= 0.001$). Orofacial clefts were also more numerous among infants exposed to corticosteroids in utero: 5 vs 1.

Event	No steroid exposure (n = 1058)	Steroid exposure (n = 432)	P value
Spontaneous Abortion (SAB)	4% (n = 39)	6% (n = 15)	0.14
Preterm birth (< 37 weeks)	8% (n = 81)	13% (n = 51)	0.008
Small for Gestational Age	4% (n = 34)	6% (n = 24)	0.03
Low Birth Weight (< 2500g)	6% (n = 54)	10% (n = 37)	0.008
Intra-Uterine Growth Retardation	2% (n = 16)	3% (n = 14)	0.03
NICU Admission	9% (n = 87)	13% (n = 50)	0.03
Any congenital malformation	9% (n = 86)	10% (n = 40)	0.37

Table 1. Pregnancy Complications in Mothers with IBD and Corticosteroid Exposure

COMMENTARY

Why Is This Important?

Corticosteroid use and IBD flares have each been associated with adverse maternal and fetal outcomes.¹ However, there is very limited data about the risk of corticosteroid use during pregnancy in IBD patients. In order to appropriately counsel IBD patients prior to conception and during pregnancy, precise data about the risks of corticosteroids, IBD flares, and medications that produce steroid-free remissions were needed. The Pregnancy in IBD and Neonatal Outcomes (PIANO) Study is the largest prospective cohort study about this topic and provides comprehensive data to address these issues. Prior reports from the PIANO Study have demonstrated no increased risk of adverse maternal or fetal outcomes with thiopurines or biologic agents.²

Key Study Findings

In the largest (n= 1,712) prospective cohort study of pregnant IBD patients, corticosteroid use was associated with an increased risk of preterm birth, low birth weight, and intra-uterine growth retardation. Both disease activity and steroid use probably contributed to these outcomes.

Caution

Again, the occurrence of IBD flares and corticosteroid use are linked, so the precise impact of steroid use vs IBD flares on pregnancy outcomes cannot be completely separated. Also, due to the self-

reporting nature of study questionnaires, specific data on dose and duration of steroid use is unavailable.

My Practice

Achieving corticosteroid-free endoscopic and clinical remission prior to conception is the goal with IBD patients. We educate our IBD patients of child-bearing age that immunomodulators and biologic agents should be used, if needed, and that these treatments should be continued during pregnancy to minimize the risk of IBD flares.² I currently do not recommend pregnancy while the patient is on a small molecules such as tofacitinib, upadacitinib, and ozanimod, all of which do not have adequate safety data for use during pregnancy. If steroids are needed to manage IBD flares during pregnancy, we focus on using the lowest possible dose for the shortest period.

For Future Research

Larger cohorts of steroid-using pregnant patients will be needed to precisely define the risk of oro-facial clefts in their infants, although available data suggests that steroids increase the risk of this congenital malformation.

Conflict of Interest

Dr. Schoenfeld has no relevant conflicts of interest. Dr. Charabaty has served as a consultant/advisory board member for AbbVie Pharmaceuticals, Takeda Pharmaceuticals, Pfizer Pharmaceuticals, Bristol Myers Squibb Pharmaceuticals, and Janssen Pharmaceuticals.

Note: The authors of the article published in *Gut* are active on social media. Tag them to discuss their work and this EBGI summary!

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