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Observations and Research

Pregnant Pause? Not for IBD Care—A Single Tertiary Care Center Prospective Cohort Study Affirming IBD Management in Pregnancy

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Background: This study examined Inflammatory Bowel Disease (IBD) management and outcomes during pregnancy in a tertiary care setting, focusing on disease activity, medication use, and maternal and neonatal outcomes.

Methods: A prospective cohort study followed 287 women with IBD through 291 pregnancies from 2017 to 2023 at a single tertiary care center, collecting data preconception, during each trimester, and postpartum.

Results: The study observed a 92.7% live birth rate. Seventy-four percent of individuals were in clinical remission preconception, and disease activity increased throughout pregnancy, particularly in ulcerative colitis (UC) patients (peaking at 37% in the second trimester), while remaining stable in CD patients. UC, disease duration <5 years, and preconception activity correlated with higher disease activity during pregnancy. Biologic use remained stable without significant impact on outcomes. Preterm delivery (6.7%) and small for gestational age infants (7%) rates reflected baseline population risk. Steroid use was associated with higher preterm delivery rates. Gestational hypertension (6.9%) and diabetes (9.4%) rates were similar to population norms. Maternal adverse events were higher in women 40 or older (OR 3.893).

Conclusions: This study reaffirms the safety of continued medical therapy for IBD throughout pregnancy in a tertiary care, prospective cohort. Increased disease activity throughout pregnancy was evident, particularly in UC. Despite higher rates of disease activity amongst those with UC, outcomes were similar in those with CD vs UC—suggesting that disease activity measures have limitations in CD and pregnancy, or there is some mild inherent risk of CD in pregnancy outcomes irrespective of disease activity.

Lay Summary

In a prospective cohort study of 291 pregnancies in women with IBD, findings demonstrated most women had healthy pregnancies, with proper medical care and monitoring. Continuing IBD medications during pregnancy was safe, though some patients experienced more active disease symptoms.

Key Words: IBD, Crohn's, ulcerative colitis, epidemiology, pregnancy

Introduction

Inflammatory Bowel Diseases (IBD) such as Crohn's disease (CD) and ulcerative colitis (UC) are chronic conditions that are often diagnosed in young adulthood, which lead to unique health challenges, including potential impact on fertility and pregnancy outcomes.

In pregnancy, active IBD has been associated with preterm labor, low birth weight, spontaneous abortion, and preeclampsia. In contrast, many studies demonstrate that women with quiescent disease in pregnancy exhibit similar pregnancy outcomes to those seen in the general population—suggesting that effective disease control prior to conception and throughout gestation is important in this population.[1–5]

The Pregnancy in Inflammatory Bowel Disease and Neonatal Outcomes (PIANO) registry has provided confidence that pregnancies exposed to anti-TNF therapy and thiopurines do not increase the risk of adverse maternofetal outcomes when compared to those not exposed to the medications.[6] Similar safety data has been demonstrated through the PIANO study for vedolizumab and ustekinumab, as well as through the CONCEIVE study for vedolizumab.[7,8] Corticosteroids, however, have been demonstrated to increase the risk of preterm birth, low birth weight, and neonatal intensive care admissions.[9–11]

Despite the established risks of active IBD, there remains a significant gap in the perception of the safety of medication in pregnancy. Survey data has indicated that nearly 25% of

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women believe it is more important to tolerate symptoms to avoid fetal exposure to IBD medication with 84% of women reporting significant concern of adverse events due to medication exposure, but only 19% identifying that active disease in pregnancy poses increased risk.[12,13]

The management of IBD is complex, with evolving treatment options in recent years. While recent studies provide valuable insights, there remains a paucity of prospective data from closely monitored, high-risk populations in specialized care settings.[14,15] This gap in knowledge is particularly significant given the potential for more severe disease courses and complex management decisions in tertiary care centers. Our study aims to address this need by providing a comprehensive analysis of IBD management and outcomes in a specialized pregnancy clinic within a tertiary care setting.

Specifically, we sought to examine several key aspects: factors contributing to disease activity throughout pregnancy and postpartum; differences in disease activity patterns between UC and CD during pregnancy; the relationship between steroid use and pregnancy outcomes; the impact of biologic therapies on maternal and fetal outcomes; and the rates and determinants of cesarean delivery. Furthermore, we aimed to assess specific pregnancy outcomes, including live birth rate, spontaneous abortion rate, preterm delivery rate, small for gestational age (SGA) infants, and maternal complications such as gestational hypertension, preeclampsia, gestational diabetes, and infections.

As our population is from a tertiary care single center, we are able to extract detailed disease activity patterns, medication use for each trimester and compliance, and pregnancy outcomes that may not be apparent in broader population studies. The longitudinal nature of our data collection allows for a detailed examination of disease trajectories throughout pregnancy and into the postpartum period, offering insights into the dynamic interplay between IBD and the physiological changes of pregnancy.

Methods

Study Design

This was a prospective cohort study performed at a single tertiary care center in British Columbia (BC), Canada. The IBD center of BC's pregnancy in IBD clinic serves the entire population of BC and some of the Yukon Territory. A prospectively designed database was initiated in 2017 and followed patients enrolled through to 2023. The database and study were approved by institutional ethics through the University of BC. All patients were approached at their first visit to the clinic and provided consent to be included in the study. All participant data was de-identified for record collection. Individuals could be enrolled multiple times in the study with subsequent pregnancies.

Patient Selection and Follow-Up

All women enrolled in the IBD Center of BC's pregnancy clinic were approached for the study. All patients seen at this clinic are followed by a standardized clinical care pathway (CCP). As part of this CCP patients are counseled on the importance of disease remission prior to conception, undergo objective testing when appropriate preconception, counseled on maintaining IBD therapies during pregnancy (with the exception of methotrexate and small molecules) and to contact the clinic's IBD nurse immediately on any symptoms or signs of disease flare. The majority of patients are seen in joint consultation by the gastroenterologist and high-risk obstetrician at least once throughout pregnancy. Participants were excluded if they were unable to provide consent, did not provide consent, or if they did not have a confirmed diagnosis of IBD. If enrollment occurred during pregnancy or the postpartum period then details were collected retrospectively for the earlier periods. Follow-up visits in the clinic were scheduled preconception, once each in the first trimester (T1), the second trimester (T2), the third trimester (T3), and once within the first 6 months postpartum with additional follow-up occurring in the event of active disease or if patient initiated. Participants were asked to complete, as part of routine standard of care, fecal calprotectin and blood work—including c-reactive protein (CRP), albumin, ferritin, hemoglobin, and a white blood cell count—to supplement the clinical assessment.

Baseline Data

Baseline demographics collected included age at disease diagnosis, age at delivery (or enrollment for those who did not go on to have a pregnancy), disease type (UC vs CD), disease phenotype, behavior, extent, and treatment, surgical history, obstetrical history, smoking status, and fertility history.

Maternal Disease Activity

Disease activity was recorded preconception, in each trimester, and postpartum as either active or inactive. This was determined using the adapted Harvey Bradshaw Index (HBI) for CD (excluding abdominal exam for disease assessment in pregnancy) and the full mayo score (FMS) or partial mayo score (PMS) for UC. Clinical disease activity was measured by HBI ≥ 5, PMS ≥ 2, and FMS ≥ 3. Moderate to severe disease activity was represented by HBI > 8, PMS > 4, and FMS > 5. In some cases, the clinical activity was labeled "active" despite a score below the above cutoffs. This was at the clinicians discretion and was based on available endoscopic data and fecal calprotectin. For patients with an ostomy or an IPAA clinical activity scores were excluded and clinician determination was used.

Medication Exposure

Medication exposure was recorded at each visit with documentation of any cessation or delay in medical therapy. Maintenance medication was recorded as (1) TNF Inhibitor; (2) TNF inhibitor combined with thiopurine; (3) Other biologic; (4) other biologic combined with thiopurine; (5) thiopurine; (6) 5-ASA therapy alone; (7) 5-ASA or steroid rectal therapy alone or; (8) no therapy. If an individual was on 5-ASA therapy combined with a biologic or immunomodulator they were included in categories 1–5. Small molecule and methotrexate use were screened for, but ultimately in our population no patients were using these medications.

Steroid use was recorded in each trimester and was inclusive of systemic corticosteroid use with prednisone, intravenous corticosteroids, or oral budesonide.

Pregnancy Outcomes

Recorded pregnancy outcomes included spontaneous abortions which were defined as pregnancy loss prior to 20

weeks gestational age (GA) without a therapeutic abortion; therapeutic abortion or pregnancy termination; stillbirth or pregnancy loss after 20 weeks GA; or completed pregnancy resulting in a live birth. If there was no recorded pregnancy within 1 year of enrollment in the pregnancy clinic this was reflected in the "no pregnancy" group.

Multiples gestations were recorded but not included in the statistical analysis of birth outcomes. Delivery records were obtained from the medical chart and method of delivery was recorded as (1) vaginal delivery, (2) elective cesarean, and (3) emergency cesarean.

Maternal Outcomes

Obstetrical records were used to document maternal outcomes throughout and following pregnancy. A composite of maternal outcomes was used for statistical analysis, which included gestational hypertension, gestational diabetes, and serious maternal infection.

Hypertension was characterized as (1) gestational hypertension or (2) preeclampsia. Gestational diabetes was diagnosed using obstetrical standards. Common infections were recorded throughout pregnancy and postpartum. Mastitis and maternal viral infections were excluded as infectious complications unless patients were hospitalized, due to subjectivity of diagnosis and difficulty confirming. Chorioamnionitis was determined based on obstetrical records. Postpartum infections requiring prolonged admission or presentation to the emergency department included cesarean wound infections, sepsis, intra-abdominal abscess, and infected retained products of conception.

Other outcomes were suspected to be less impacted by IBD medication or disease activity and were not included in analysis but were descriptively reported. These include pregnancy-related non-IBD liver concerns, placental anomalies, postpartum hemorrhage, oligohydramnios, and polyhydramnios.

Neonatal Outcomes

Preterm birth

The rate of any preterm delivery was defined as any delivery prior to 37 weeks GA. This was further stratified into moderately preterm (32-37 weeks GA), very preterm (28-32 weeks GA), and extremely preterm (<28 weeks GA).

Small for gestational age

To accommodate for the effect of GA on birth weight at delivery, the rate of infants born SGA was analyzed, rather than low birth weight alone. This was defined as a birth weight below the 10th percentile for GA using Canadian reference data.

Congenital anomalies

Congenital anomalies were reviewed at the postpartum appointment based on the 12 categories of congenital anomalies captured by ICD 10 codes.

Infections in the first 6 months of life were documented at each postpartum check. This was based upon the mother's report of the type of infection as well as need for hospitalization or systemic antibiotics.

Statistical Analysis

Statistical analysis was performed using IBM SPSS software version 29. Descriptive statistics, including means, standard deviations, and percentages, were used to summarize demographic and clinical characteristics. Categorical variables were compared using chi-square tests or Fisher's exact test when expected cell counts were low. Univariate and multivariate logistic regression analyses were conducted to assess factors associated with various outcomes, with odds ratios (ORs) and 95% CIs reported to quantify the strength of associations. Temporal changes in medication use and disease activity were analyzed using Cochran's Q test and McNemar's test for paired nominal data. Continuous variables, such as fecal calprotectin levels, were compared between groups using *t*-tests or Mann–Whitney *U* tests and across multiple time points using ANOVA or Kruskal–Wallis tests. Throughout the analysis, *P*-values <.05 were considered statistically significant.

Results

Women attending the IBD in pregnancy clinic from January 1, 2017, to December 31, 2023 were recruited for enrollment. Of the 311 approached for inclusion, 27 were excluded. Of the 287 patients enrolled in the study, 3 were lost to follow-up before any pregnancy outcomes were observed and 50 went on to have no pregnancy within 1 year. Ultimately, 243 individuals were followed through 291 pregnancies with 275 live births.

Baseline Characteristics

Baseline characteristics can be seen in Table 1. Of the 344 cases enrolled in the study, 194 women had UC, 147 had CD, and 3 had indeterminate colitis (counted as UC for statistical analysis). The average age at diagnosis was 23.78 years old, and the average disease duration was 8.88 years. The average age at delivery was 32.79 years, with no women under 20 or over 50 at delivery. The average BMI was 24.32. Most participants were Caucasian, followed by South Asian and then East Asian.

Two hundred and twelve (62%) women were nulliparous at enrollment. 63 (18%) reported previous fertility difficulties with >1 year to conception, while 55 (16%) reported consulting with a fertility specialist. The majority of participants had never smoked.

No Conception within 1 Year

A total of 50 women did not conceive within 1 year of enrollment. No significant difference in conception was observed based on the type of IBD, Smoking status, BMI, preconception disease activity, or prior difficulty with conception (Table S1). Nulliparous women were more likely not to conceive within 1 year from enrollment than those who had previously had children (OR 2.500, 95% CI 1.232-5.076).

Pregnancy Outcomes

Pregnancy outcomes excluded twin pregnancies for statistical analysis. Overall, there were 5 multiple gestation pregnancies and 286 singleton pregnancies, which resulted in 17 (6%) spontaneous abortions, 2 (0.7%) therapeutic abortions, 2 (0.7%) stillbirths, and 265 live singleton births (92.7%).

In univariate analysis, there was no statistically significant association in the rate of spontaneous abortion and the type of IBD, preconception disease activity, or previous spontaneous abortions (Table S1). The rate of stillbirth was rare and further analysis was not possible.

Table 1. Patient characteristics.

		Total *N* = 344 (%)	UC *N* = 197 (%)	CD *N* = 147 (%)
Age Category	<17	44 (13)	12 (6)	32 (21)
	17-40	302 (87)	184 (94)	118 (79)
	>40	0	0	0
Average age at diagnosis		23.78	25.02	22.13
Age at Delivery	*N* = 270	32.79	32.64	33.02
Disease Duration				
BMI	*N* = 265	24.32	24.22	24.44
Disease Location	Ileal		–	49
	Colonic		–	37
	Ileocolonic		–	57
	Proctitis		37 (21)	–
	Left sided		74 (41)	–
	Pancolitis		68 (38)	–
Disease Behavior	Inflammatory		–	84 (57)
	Stricturing		–	35 (24)
	Penetrating		–	20 (14)
	Perianal modifier		–	26 (18)
Previous Surgeries	Resection	41		
	Colectomy	16		
	Perianal Surgery	9		
	Diverting Ostomy	1		
Age at Delivery	20-24	14 (5)	9 (6)	5 (5)
	25-29	70 (26)	42 (26)	28 (25)
	30-34	116 (43)	68 (43)	48 (44)
	35-39	59 (22)	36 (23)	23 (21)
	40-44	8 (3)	4 (3)	4 (4)
	45-49	3 (1)	1 (1)	2 (2)
Disease Duration		8.88	7.48	10.75
Ethnicity	Caucasian		97	79
	East Asian		13	2
	Indigenous		3	0
	Latin American		2	2
	Middle Eastern		7	7
	Other		5	6
	South Asian		28	16
	Missing		46	39
Smoking Status	Never	302 (90)	183 (94)	119 (86)
	Current	13 (4)	1 (1)	12 (8)
	Previous	19 (6)	10 (5)	9 (6)
Consulted with fertility specialist?		52	37	15
>1 Year to conceive		64	34	30
Preconception Medication	TNF Inhibitor	111 (32)	46 (23)	65 (44)
	Ustekinumab	17 (5)	3 (2)	14 (10)
	Vedolizumab	37 (11)	26 (13)	11 (7)
	Thiopurine	17 (5)	7 (4)	10 (7)
	5-ASA alone	65 (19)	52 (26)	13 (9)
	Rectal alone	15 (4)	15 (8)	0
	TNF + Thiopurine	21 (6)	9 (5)	12 (8)
	Other biologic + Thiopurine	5 (1)	2 (1)	3 (2)
	No medication	56 (16)	37 (19)	19 (13)
Preconception Steroids		14 (4)	11 (6)	3 (2)

Table 2. Neonatal outcomes in pregnancies with IBD: breakdown between UC and Crohn's disease (CD).

Outcome	Total	UC	CD
Number of Singleton Live Births	265		
Male	124	81	43
Female	99	58	41
Mean birth weight (SD)	3.304 (0.53)	3.296 (0.56)	3.318 (0.48)
Birth weight Category			
< 2500	13 (6)	10 (7)	3 (4)
> 2500	214	134	80
Small for Gestational Age	17 (6)	13 (9)	4 (5)
Mean Gestational Age (SD)	38.68 (1.63)	38.66 (1.61)	38.72 (1.67)
Term at Delivery			20
Term	221	139	82
Moderate to Late Preterm	14	8	6
Very Preterm	2	1	1
Extremely Preterm	0	0	0
Congenital Anomalies	7	2	5
Number of Multiples Live Births	10	6	4

Method of Delivery

Cesarean delivery was seen in 51% of pregnancies. In univariate analysis, higher rates of CS delivery were seen in primiparous pregnancies (OR 1.781, 95% CI 1.052-3.016). Those with UC (OR 0.52, 95% CI 0.304-0.889 vs CD) and those under 40 at delivery (OR 0.237, 95% CI 0.035-0.862) were less likely to undergo CS delivery. When carried forward to multivariate analysis both parity and age remained significant, while the association between type of IBD and cesarean delivery was attenuated (Table S2).

Perianal disease history and disease activity throughout pregnancy were not found to be significantly associated with the rate of CS delivery with respective ORs of 2.49 (CI 0.848-7.306) and 1.26 (CI 0.751-2.104).

Maternal Outcomes

Gestational hypertension occurred in 17 out of 245 pregnancies (6.9%). Of these cases, 12 were gestational hypertension without progression and 5 developed preeclampsia. Gestational diabetes was observed in 9.4% of pregnancies (23/244) and infection in 4.9% (12/244).

In total, maternal complications occurred in a total of 84 pregnancies and can be found in Table S2. The most common of these were gestational diabetes (n = 23), gestational hypertension (n = 17), and postpartum hemorrhage (Table S3).

The composite outcome of gestational hypertension, gestational diabetes, or maternal infection was seen in 49 cases (20%). Univariate analysis found no significant association between maternal adverse events and steroid exposure, disease activity throughout pregnancy, or biologic exposure. Maternal adverse outcomes were less common among those with UC, with a trend toward significance (OR 0.583, 95% CI 0.310-1.097), and those age 40 or older at delivery were significantly more likely to experience maternal adverse events (OR 3.896, 95% CI 1.339-11.337). Multivariate analysis confirmed the association with age. The risk associated with type of IBD was not significant in multivariate analysis (Table S4).

Neonatal Outcomes

The study reported a total of 265 singleton live births, though the birth records were incomplete or missing in 27 cases (Table 2). Overall, there were 124 male and 99 female infants. The mean birth weight was 3.304 kg with 13 infants weighing less than 2500g at delivery and 17 infants born SGA. The mean GA was 38.68 weeks. The majority of deliveries were at full term. Of the 16 (7%) preterm deliveries, 14 infants born late preterm (32-37 weeks) and 2 infants born very preterm (28-32 weeks). Congenital anomalies were seen in 7 infants (2 in UC and 5 in CD). Additionally, the study included 5 twin pregnancies with 10 live infants (6 UC and 4 CD).

Preterm Birth

Delivery prior to 37 weeks GA was seen in 16 cases (6.7%). No infants were born prior to 28 weeks GA (extremely preterm), and only 2 were born between 28 and 32 weeks GA. Steroid exposure throughout pregnancy correlated with an elevated rate of preterm delivery, with 20% of those exposed to corticosteroids born preterm (P = .001). Those with moderate to severe disease throughout pregnancy had a 12% rate of preterm delivery, while those without had only a 6% rate. This did not meet statistical significance (Table S5).

Small for Gestational Age

17 infants were born SGA (7%). There was no statistical difference between type of IBD or disease activity.

Infant Infections

Complete postpartum data up to 6 months was available for 151 infants. Infections were reported in 20 infants (13%). Of these, 13 (9%) required antibiotics. Four (3%) were hospitalized due to the infection and 2 (1%) others required the neonatal intensive care unit due to the infection. Table S6 outlines the details of these cases. Univariate analysis suggested a correlation between biologic exposure and infections in the first 6 months of life (OR 6.58, 95% CI 2.12-20.40, P < 0.001). Given the small number of outcomes

and the number of missing results, propensity score matching was undertaken to account for possible confounding by disease activity, preterm delivery, and steroid exposure. After matching, there was a significantly higher rate of infections among bio exposed infants compared to nonexposed (25% vs 6.2% $P = 0.003$).

Disease Activity

Among those with active disease, fecal calprotectin was significantly higher than among those with inactive disease at every stage from preconception to postpartum (Table S6 and Figure S4). CRP was similarly elevated in those with active disease, but this was not significant in the preconception time frame. In the active disease group, fecal calprotectin peaked in T2 at a mean of 1128.

Although CRP levels increased during pregnancy even in patients with inactive disease, they remained notably lower than in those with active disease. The peak CRP values were 13.6 in the active disease group (during T3) and 6.7 in the inactive disease group (during T2).

CD activity was identified at a stable proportion in the preconception period, throughout pregnancy, and postpartum (22% preconception, 24% T1, 24% T2, 19% T3, 22% postpartum). However, moderate to severe activity identified by HBI > 8 was identified in very few patients with CD. This was stable throughout pregnancy, though did occur in a higher proportion of patients postpartum (3% preconception, 3% T1, 3% T2, 2% T3, 5% postpartum) (Figure 1).

Preconception 26% of UC patients had active disease—this increased throughout pregnancy and postpartum, with a peak in T2 (32% TI, 37% T2, 32% T3, 32% postpartum). The rate of moderate to severe disease followed a similar trend, but with a more significant decrease (to lower than preconception rates) in T3 (Figure 2).

Univariate and multivariate analysis were done to explore the factors contributing to disease activity throughout pregnancy. In univariate analysis, active disease in pregnancy was seen more frequently in those with UC than CD (OR 2.169, $P < .001$) and in those with preconception disease activity (OR 7.629, $P < .001$). Disease duration > 5 years (OR 0.592, $P < .001$) and adherence to preconception medication (OR 0.539, $P = .03$) both demonstrated protective effects. These remained significant in multivariate analysis with the exception of preconception medication use, which had an attenuated impact (OR 0.919, $P = .810$) (Table S7).

Similarly, among the 103 participants with active disease postpartum, univariate analysis suggested an association with UC (OR 1.855, $P = .05$); preconception disease activity (OR 4.767, $P < .001$); and disease activity throughout pregnancy (OR 4.570, $P < .001$). Disease duration did not have a significant effect on postpartum disease activity. Medication discontinuation in the preconception period and throughout pregnancy did not have a significant association.

The relationship between disease type and postpartum disease activity was not found to be significant in multivariate analysis, though in UC vs CD the adjusted OR for

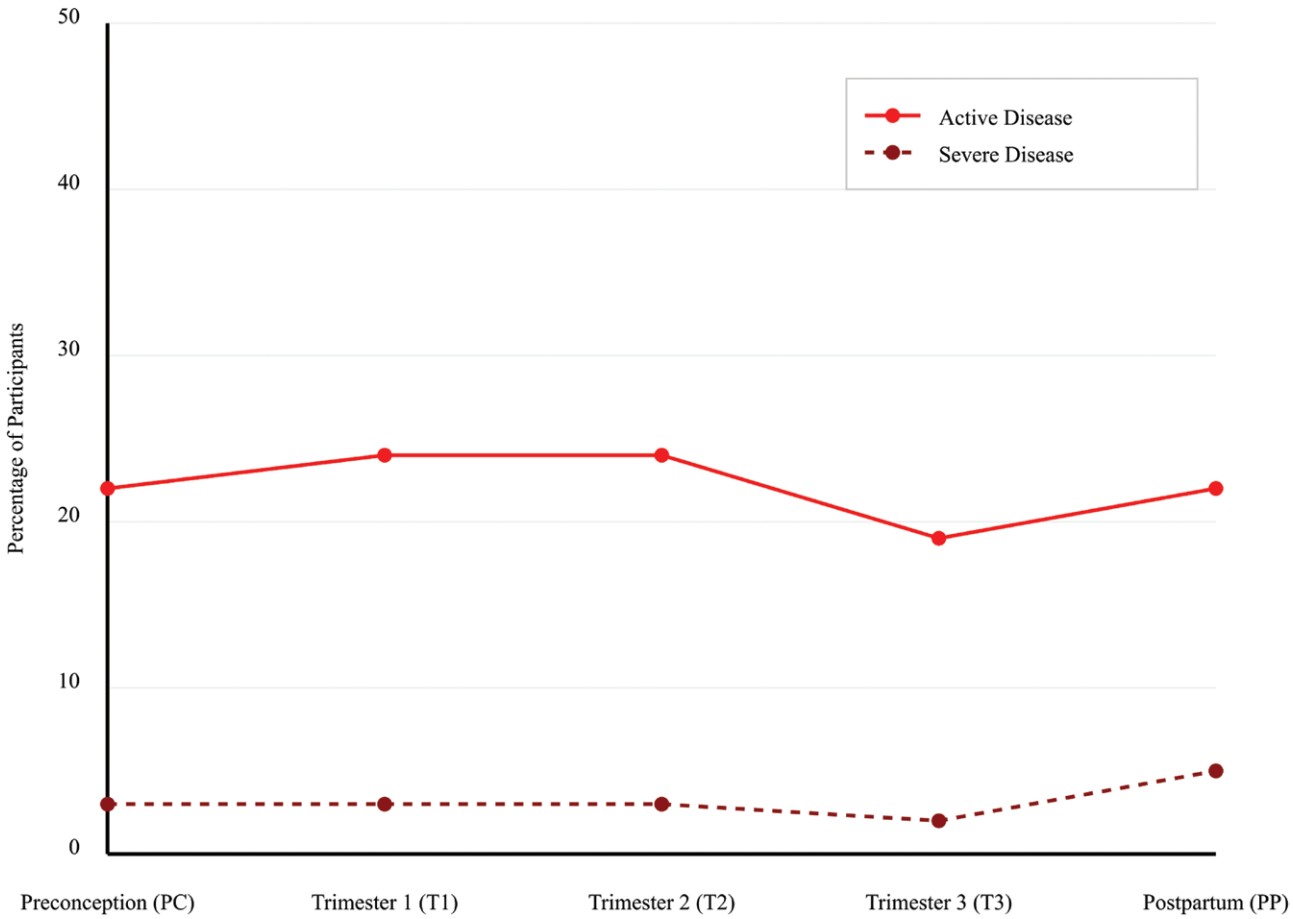

Figure 1. Rate of active and severe Crohn's disease across pregnancy stages.

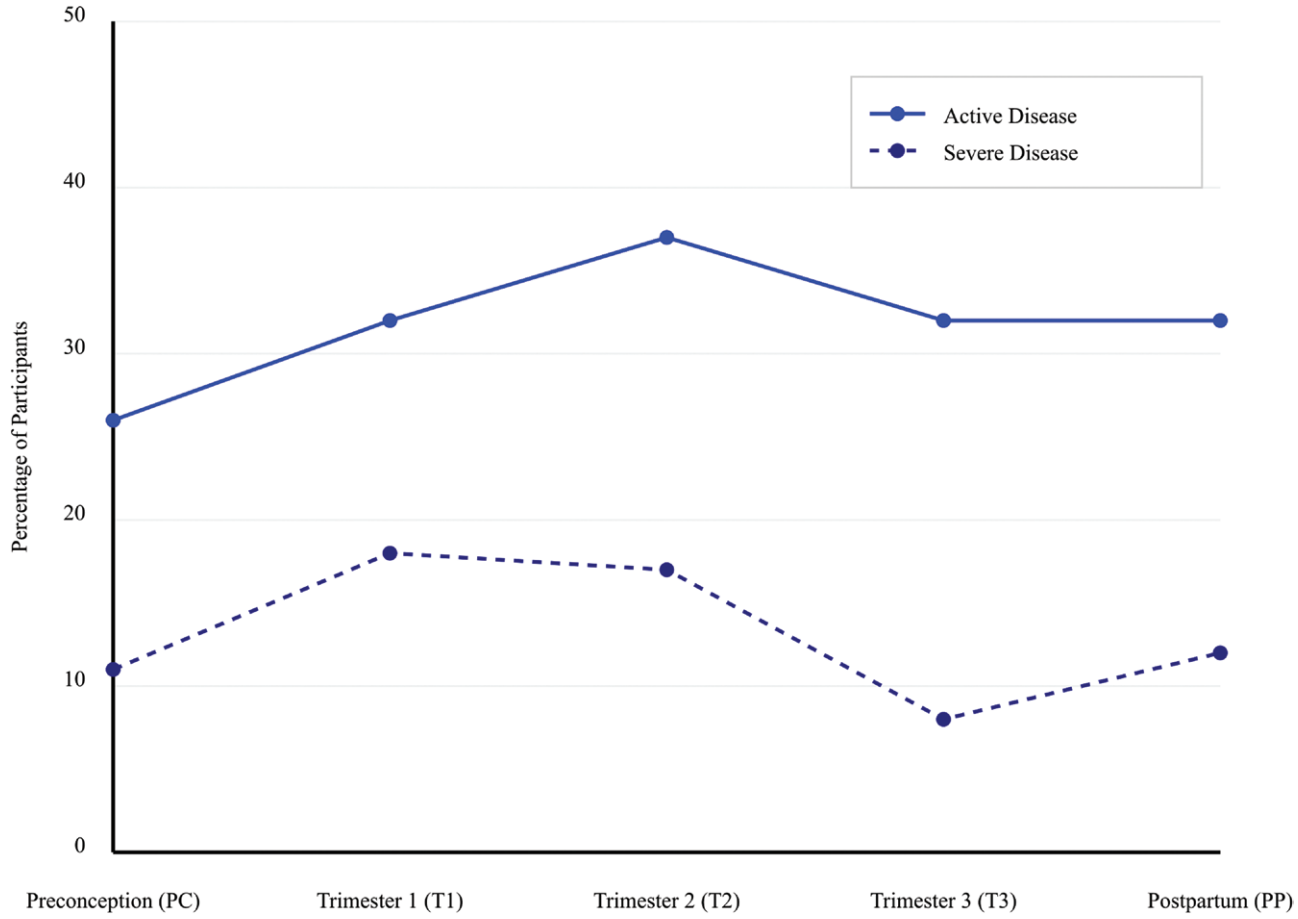

Figure 2. Rate of active and severe UC across pregnancy stages.

preconception activity was 2.996 $P = .003$ and for activity throughout pregnancy was 2.846 $P = .003$ (Table S8).

Steroid Use

Steroid use throughout pregnancy is shown in Figure S2. Prior to conception, only 4% of patients required corticosteroids (6% UC; 2% CD)—this rate increased throughout pregnancy with peak of 11% in T3 (13% UC; 7% CD). There is a significant increase in steroid use throughout pregnancy and postpartum (Cochran's Q = 26.231, $P < .001$). This is not significant when comparing T1 to the preconception period. However, it remains significant when comparing the rate in T2, T3, and postpartum to the preconception rate ($P < .001$, $P < .001$, $P = .003$ respectively). When examining this trend for those with UC, the increase in steroid use throughout pregnancy remains significant ($P < .001$). Among those with CD, the increase in steroid use throughout pregnancy and postpartum was not found to be significant ($P = .06$).

Maintenance Medication Use

In our population the total rate of TNF inhibitor use was roughly stable throughout pregnancy, with an increase in the postpartum period. Most patients on biologics continued therapy without interruption in the dose. However, 10 patients had stopped TNF inhibition between 27 and 33 weeks GA in T3 due to previous practice norms, and all 10 of these patients re-started in the postpartum period. Other biologics (vedolizumab and ustekinumab) were used by 15.7% of patients preconception, with minor fluctuations during pregnancy, ending at 15.6% postpartum. Throughout pregnancy a total of 47 patients were exposed to vedolizumab and ustekinumab. Figure S3 demonstrates the proportion of patients on each medication throughout pregnancy.

Immunomodulator use decreased from preconception, throughout pregnancy, and postpartum ($P < .001$, Cochran's Q = 36.44). Combination TNF + immunomodulator decreased from 6.1% preconception to 2.5% postpartum, while combination immunomodulator and other biologics decreased from 1.5% to 0.4% and immunomodulation alone decreased from 4.9% to 3.4%. No new thiopurine starts occurred during pregnancy.

The use of oral 5-ASA alone showed an increasing trend, beginning at 18.9% preconception and rising consistently to 24.6% postpartum ($P < .001$, Cochran's Q = 16.056). This was predominantly among UC patients, but a limited number of CD patients with colonic disease remained on 5-ASA. Rectal therapy alone was minimally used, starting at 1.5% preconception and reducing to 0.4% postpartum. Finally, the percentage of patients on no IBD maintenance therapy decreased throughout pregnancy from 16.3% preconception to 12.3% postpartum, though this change was not statistically significant ($P = .373$).

Of those who were biologic naïve preconception, 6 patients initiated biologic therapy throughout pregnancy (2 in T1, 1 in T2, 3 in T3). All of these were TNF inhibitors. Postpartum, another 3 patients required biologic therapy induction—one

with a TNF inhibitor, one with vedolizumab, and one with ustekinumab.

Surgeries

Throughout pregnancy, 3 patients underwent surgery for IBD-related issues. Among the CD population, the 2 patients required incision and drainage of perianal abscesses—one in T2, and one in T3. One patient with UC and an end ileostomy required surgery in T2 for a parastomal hernia with resultant incarcerated small bowel. One patient with UC required a colectomy in the postpartum period for high-grade dysplasia on the first postpartum surveillance colonoscopy (Table 3).

Hospitalizations

Throughout pregnancy, 7 patients required hospitalization for their IBD. In those with CD one had an intra-abdominal phlegmon, and one required dilation of a stricture. In the 5 patients with UC requiring hospitalization throughout pregnancy, 3 had acute severe colitis and 2 had previously had colectomies but were hospitalized with ostomy complications.

An additional 3 patients were hospitalized in the postpartum period. Two of these hospitalizations were for further workup of abdominal pain in patients with CD and one hospitalization was for severe anemia due to active UC (Table 4).

Discussion

This study of IBD in pregnancy at a tertiary care center provides valuable insights into the complex interplay between IBD and pregnancy outcomes in a high risk, tertiary care population.

The overall favorable pregnancy outcomes in our cohort, with a 92.7% of pregnant women going on to have a live birth rate and only 6.7% experiencing preterm deliveries, are particularly noteworthy given the high-risk nature of our tertiary care population. These results are especially encouraging when compared to the background preterm delivery rate of 8.1% in BC.[16] This also further challenges historical notions that IBD inherently leads to poor pregnancy outcomes and suggest that with meticulous management, women with IBD can achieve pregnancy outcomes comparable to the general population.[17,18] This underscores the importance of preconception counseling and achieving remission prior to pregnancy.

Disease Activity and Medication Use

Our observation of increasing disease activity throughout pregnancy, particularly in UC patients, is a key finding that deserves careful consideration. The vast majority of our patients were in remission preconception and continued their

Table 3. Surgery type, indication, and relationship to disease activity throughout pregnancy for Crohn's disease and UC.

Crohn's disease		
Surgery	**Trimester**	**Disease activity through pregnancy?**
Incision and drainage	2nd trimester	Yes
Incision and drainage	3rd trimester	Yes
Ulcerative colitis		
Surgery	**Trimester**	**Disease activity through pregnancy?**
Hernia revision and SB resection	3rd trimester	Yes
Colectomy	Postpartum	Yes—Moderate to severe

Table 4. Hospitalization indication, timing, and disease activity throughout pregnancy in Crohn's disease and UC.

Crohn's disease		
Reason for hospitalization	**Trimester**	**Disease activity through pregnancy?**
Stricture requiring endoscopic dilation	3rd trimester	Yes
Phlegmon	3rd trimester	Yes
Abdominal pain	Postpartum	No
Abdominal pain	Postpartum	Yes—Moderate to severe
Ulcerative colitis		
Reason for hospitalization	**Trimester**	**Disease activity through pregnancy?**
Acute severe colitis	1st trimester	Yes—Moderate to severe
Acute severe colitis	1st trimester	Yes—Moderate to severe
Small bowel obstruction	2nd trimester	Yes
Acute severe colitis	2nd trimester	Yes—Moderate to severe
Parastomal hernia	3rd trimester	Yes
Anemia due to active disease	Postpartum	Yes

therapy with no delay in dosing. The peak in UC disease activity (37% of patients) during T2, presents an intriguing pattern that warrants further investigation. The subsequent decrease in disease in third trimester may reflect the changes in therapy that are likely to occur in a closely monitored population when disease activity is seen to increase in pregnancy. This data is in keeping with a 2023 registry study out of Israel suggesting increased rates of disease activity in UC more than CD, with a peak later in pregnancy.[14]

The factors influencing disease activity throughout pregnancy and postpartum emphasize the importance of preconception disease assessment. Disease activity through pregnancy was found to be significantly associated with having UC, preconception disease activity, and disease duration less than 5 years. Postpartum, similar factors influenced disease activity, with preconception activity and disease activity during pregnancy being significant predictors. Interestingly, the association between disease type and postpartum disease activity was attenuated in multivariate analysis. These findings underscore the critical importance of achieving disease control before conception and maintaining it throughout pregnancy. We would recommend closer monitoring in UC particularly for those with shorter disease duration, and a history of recently active disease. The persistent influence of pregnancy disease activity on postpartum flares also emphasizes the need for continued vigilance and potentially more proactive management in the postpartum period, especially for those with active disease during pregnancy. These insights should inform individualized care plans and risk stratification for pregnant women with IBD, potentially improving both short-term pregnancy outcomes and long-term disease control.

Medication discontinuation in the preconception period and throughout pregnancy did not have a significant association with postpartum disease activity. Our study included any discontinued maintenance medication in this category, and this number would include patients who discontinued one maintenance therapy and started another within the same trimester. It would also include those who discontinued an immunomodulator but continued other combination medication. Given the small number of individuals who completely discontinued a medication during pregnancy (8 total) and the variation in timing, the impact of medication discontinuation alone may be better studied with a larger sample size or with a future case–control study design.

The differential pattern between UC and CD highlights the need for disease-specific monitoring and management strategies during pregnancy. The low rate of moderate to severe CD activity in our population is mirrored by the low rate of steroid use in CD. Given the previously documented association between active disease and adverse outcomes in pregnancy, it would be reasonable to presume that the population with CD in our study would have a lower rate of adverse outcomes than those with UC as there is a very low and stable rate of moderate to severe disease activity among the CD population. However, pregnancy outcomes were similar in those with UC and CD. Furthermore, previous studies have suggested that CD carries a higher rate of preterm delivery and SGA infants than UC despite the thought that UC seems to have more disease activity throughout pregnancy.[4,19–22] In our study, for example, the rate of preterm delivery was similar between UC (6%) and CD (8%) despite a higher rate of disease activity among those with UC. It is possible that the indices used to measure disease activity in pregnancy could underestimate disease activity in CD or overestimate in UC. It is also possible that there is something inherent about CD that increases the risk of these outcomes in pregnancy—independent of disease activity. This is a question that our current study was not equipped to answer and is worth more investigation.

The majority of surgeries and hospitalizations were among those with active disease. It is notable, however, that despite the need for IBD-related hospitalization 2 patients with CD and one with UC met clinical disease activity criteria for "mild" disease rather than moderate to severe. Similarly, both patients with CD who required surgical intervention throughout pregnancy met clinical criteria for "mild" disease. This emphasizes the limitations of clinical disease activity scores in IBD and pregnancy.

The strong association between steroid use and preterm delivery (20% vs 4%, $P = 0.001$) stands out. We suspect that the increase in disease activity accounts for this elevated rate of preterm delivery.

Our data on biologic therapies provide reassuring evidence for their continued use during pregnancy. This includes 47 patients exposed to vedolizumab or ustekinumab throughout pregnancy. This suggested safety is in keeping with the results of the CONCEIVE study and other cohort studies.[8,23] The small subset of patients who discontinued TNF in their third trimester likely represents the practice at the initiation of our study—which has since been largely abandoned due to increasing safety evidence.

Maternal Outcomes

Our analysis of delivery methods yielded intriguing results. The baseline rate of cesarean delivery in our population was 51%, which is higher than the rate of cesarean delivery noted in the population of BC (40.2% in 2021), and the rate seen in the PIANO study population (44%).[6,24] Similar Canadian tertiary care studies have also demonstrated a CS rate of 52% for CD and 48% for UC, which is in keeping with the rate described in our study.[25] Notably, within the Canadian population the rate of CS delivery is highest within the province of BC (31.2% in Canada, 40.2% in BC in 2021), and the rate of CS delivery has been notably higher in studies of those with IBD compared to those without (44% vs 32% PIANO study).[6,16] This rate likely reflects both the practices in BC and the increased rate of CS in the IBD population. The rate of vaginal delivery among patients with CD remained lower than those with UC even when perianal disease was controlled for. This suggests that factors beyond perianal disease activity may influence obstetrical decision-making in CD patients and warrants further investigation.

The maternal outcomes in our cohort, particularly the rates of gestational hypertension (6.9%) and gestational diabetes (9.4%), are relatively reassuring when compared to both the general Canadian population and previous IBD-specific studies. The rate of gestational hypertension in our cohort is comparable to the reported rate of 7-8.8% in the general Canadian population.[24] Similarly, our observed rate of gestational diabetes aligns closely with the increasing rate of gestational diabetes seen in Canada within our study time frame (9%-12% from 2017 to 2022).[24] These findings are also consistent with the PIANO study, which reported no significant increase in hypertensive disorders or gestational diabetes

in women with IBD compared to controls.[6,7] However, the increased risk of adverse maternal events in women aged 40 or older (OR 3.896, 95% CI 1.339-11.337) is a critical finding that warrants attention. This age-related risk, which persisted even after controlling for disease activity and medication use, aligns with the general trend of increased pregnancy complications in advanced maternal age.[26] This suggests that maternal age should be a key consideration in risk stratification for IBD pregnancies, potentially amplifying the already complex risk profile of these patients. Future research should aim to develop and validate risk prediction models that incorporate maternal age along with IBD-specific factors to better guide management strategies.

Neonatal Outcomes

Our findings on neonatal outcomes, particularly the relatively low rate of SGA infants (7%), provide reassurance about fetal growth in IBD pregnancies. This rate is comparable to the general Canadian population rate of 8.6% and that reported in a UK tertiary care center registry (6.3%), and lower than the rate reported (9.8%) in a 2021 meta-analysis of 9 studies of IBD in pregnancy outcomes.[4,15,16]

While our study suggests a significant association between biologic exposure and infant infections in the first 6 months of life, several limitations warrant consideration. The small sample size (151 infants) and low number of infection events (20 cases) limit statistical power and preclude comprehensive multivariate analyses, including subgroup analyses by biologic type. Propensity score matching addressed some confounding factors, but unmeasured confounders may still exist. Retrospective data collection could introduce recall bias, particularly for minor infections. Although 65% of reported infections required antibiotics, the long-term clinical significance remains unclear, and very few infections resulted in hospitalization. While many studies have not found an elevated rate of neonatal infections in infants exposed to biologics, a 2022 French study did suggest that there may be a higher rate of infection among infants born to mothers on combination therapy.[6,27] Future larger-scale studies are needed to address these limitations and provide more definitive conclusions on the relationship between biologic exposure and infant infections.

The lack of association between SGA and disease activity in our study was unexpected and contrasts with some previous studies, including a meta-analysis by Kim et al. which found a significant association between active IBD and SGA (OR 1.48, 95% CI 1.19-1.85).[4] This discrepancy could be due to our tertiary care setting, where aggressive management might have mitigated the impact of disease activity on fetal growth. The PIANO study similarly found no significant increase in SGA among infants exposed to biologics or immunomodulators, suggesting that well-controlled disease may negate this risk.[6,7] Alternatively, our findings could suggest that the relationship between IBD activity and fetal growth is more complex than previously thought, possibly mediated by factors we did not measure, such as nutritional status or placental function.

Conclusions

The hospitalization and surgery data from our cohort provide valuable insights into the most severe complications of IBD during pregnancy. The fact that all participants requiring surgery had active disease throughout pregnancy underscores the importance of achieving and maintaining remission before and during pregnancy. However, the discrepancy between clinical disease activity scores and the need for hospitalization or surgery, particularly in CD patients, further highlights the limitations of these scoring systems in pregnancy.

Our study's strengths lie in its prospective design, detailed longitudinal follow-up, and comprehensive assessment of both maternal and neonatal outcomes. The focus on a tertiary care center allowed for the examination of a higher-risk population, providing insights that are particularly relevant for complex cases. However, this also represents a limitation in terms of generalizability to all healthcare settings.

Several areas warrant further investigation based on our findings. First, the mechanisms underlying the differential disease activity patterns in UC and CD during pregnancy should be explored, potentially through studies of the pregnancy-related changes in the gut microbiome and mucosal immune system. Second, the development of pregnancy-specific disease activity indices that correlate better with outcomes like hospitalization and surgery could be beneficial. Third, long-term follow-up studies of children born to mothers with IBD, particularly those exposed to biologics in utero, would provide valuable data on the long-term safety of these medications.

In conclusion, our study provides a detailed assessment of IBD management and outcomes in pregnancy within a Canadian tertiary care setting. The overall favorable outcomes are encouraging, but the increase in disease activity, particularly in UC, and the risks associated with steroid use and disease activity highlight ongoing challenges. Our findings support the continued use of biologic therapies and emphasize the need for vigilant monitoring and personalized treatment strategies throughout pregnancy and the postpartum period.

Supplementary Data

Supplementary data are available at *Crohn's & Colitis 360* online.

Author Contributions

E.S. Data cleanup and analysis, final data collection, writing the paper; Y.L. conceived the idea and designed the database and study. Y.L. was primarily responsible for patient recruitment and data collection. B.B; G.R; and E.J. all contributed to the initial study design and patient recruitment, with ongoing input into study implementation. N.K. and V.C. contributed to data collection. S.M. contributed to reviewing and editing.

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Conflicts of Interest

E.S. has received honoraria from AbbVie; B.B. has been an advisor and/or speaker for AbbVie, Allergan, Amgen, Celgene, Ferring Pharmaceuticals, Genentech, Janssen, Merck, Microbiome Insights, Pendopharm, Pfizer, Protagonist, Shire, and Takeda; has received research support from AbbVie, Alvine,

Amgen, Atlantic Pharmaceuticals, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Genentech, GSK, Janssen, Merck, Qu Biologic, RedHill Biopharma, and Takeda; and holds stock options in Qu Biologic; Y.L. has received honoraria for Advisory Board participation and speaker fees from Janssen, Abbvie, Takeda, Pfizer, and Merck; G.R. has received honoraria from Abbvie, Frensius-Kabi, Janssen, Pfizer, Takeda, Merck, Amgen, Viatris, Organon and Ferring as a speaker, adviser and consultant. Research Grant support from Abbvie, Fresnius-Kabi, Ferring and Crohn's and Colitis Canada. SM, NK, VC, and EJ have no conflicts to disclose.

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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