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Longitudinal Trends in Pregnancy Outcomes Among Women With Inflammatory Bowel Disease in the Era of Biologics: A 20-Year Nationwide Analysis

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Background: Many women with inflammatory bowel disease (IBD) are diagnosed by their reproductive years. Prior literature suggests that women with IBD may be at increased risk of adverse pregnancy outcomes. Biologics have revolutionized IBD treatment, and current evidence favors continuation during pregnancy. We sought to examine trends in pregnancy outcomes over 20 years with the evolution of IBD treatment.

Methods: Using the National Inpatient Sample, IBD and non-IBD obstetric hospitalizations were identified between 1998 and 2018 using International Classification of Diseases 9 and 10 codes. Outcomes of interest included cesarean delivery, gestational diabetes, preeclampsia/eclampsia, premature rupture of membranes (PROM), preterm delivery, fetal growth restriction (FGR), fetal distress, and stillbirth. Stratified by Crohn's disease (CD), ulcerative colitis (UC), and non-IBD deliveries, temporal trends and multivariable logistic regression were analyzed.

Results: There were 48 986 CD patients, 30 998 UC patients, and 69 963,805 non-IBD patients. Between 1998 and 2018, CD deliveries increased from 3.3 to 12.9 per 10 000 deliveries ($P < 0.001$) and UC deliveries increased from 2.3 to 8.6 per 10 000 deliveries ($P < 0.001$). Cesarean deliveries, gestational diabetes, preeclampsia/eclampsia, PROM, FGR, and fetal distress increased over time for IBD and non-IBD women, while preterm deliveries decreased ($P < 0.001$). Multivariable analyses demonstrated that IBD patients had higher risk of cesarean delivery, preeclampsia/eclampsia, PROM, and preterm delivery compared with non-IBD patients.

Conclusion: Over a 20-year period, live deliveries amongst women with IBD have increased. Trends in pregnancy outcomes have followed a similar trajectory in patients with and without IBD. However, there is still demonstrable risk of adverse pregnancy outcomes in patients with IBD.

Lay Summary

In this study examining pregnancy trends over 20 years, the proportion of live deliveries amongst women with IBD increased steadily. Despite advances in treatment, we found that IBD still confers a higher risk for many adverse pregnancy outcomes.

Key Words: Crohn's disease, ulcerative colitis, inflammatory bowel disease, pregnancy, maternal-fetal outcomes

Introduction

Inflammatory bowel disease (IBD) is a chronic, relapsing inflammatory disorder of the gastrointestinal tract that impacts individuals across the age spectrum.[1] The prevalence of IBD has been rising over the years, and about half of those diagnosed with IBD are women.[1–3] Most women with IBD carry this diagnosis during their reproductive years and are subject to the impacts of disease on their pregnancy course and outcomes.[3]

Most women with IBD have a normal pregnancy course and delivery[4]; however, prior studies have illustrated increased risks imposed by a diagnosis of IBD for both mothers and their newborns. A large 2015 Danish cohort study demonstrated a higher likelihood of severe preeclampsia, preterm premature rupture of membranes (PPROM), medically indicated preterm delivery in women with IBD, and a 2-fold increase in low Apgar scores in term infants born to mothers with IBD.[5] Heightened risks of adverse obstetric outcomes were also described in a 2005 study using nationwide hospital data, in which women with IBD had higher odds of cesarean delivery, venous thromboembolism, and need for blood transfusion compared with women without IBD.[6] Additionally, a large meta-analysis of 23 cohort studies involving over 15 000 patients with IBD found a higher odds ratio of preterm birth, small for gestational age (SGA) birth weight (defined as below the 10th percentile for the gestational age), and stillbirth compared with non-IBD patients.[7]

The elevated risk of adverse pregnancy outcomes in IBD has mainly been attributed to active disease at conception or disease flares during pregnancy.[4,8] Other predictors of

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Key Messages

- Prior literature has demonstrated that women with IBD are at risk of adverse pregnancy outcomes. However, little is known about trends in IBD pregnancy outcomes since the advent of biologic therapy.
- Between 1998 and 2018, live deliveries in IBD patients steadily increased. However, IBD still confers a statistically increased risk in many adverse pregnancy outcomes despite advances in treatment.
- Our work highlights that pregnant patients with IBD remain at risk for adverse pregnancy outcomes. Further work is needed to address factors affecting disease control at the time of pregnancy and to understand other factors beyond disease control that may be affecting pregnancy outcomes.

adverse outcomes have included poor nutrition, medication exposures, anemia, and prior IBD-related surgeries.[4,9] A large 2014 Swiss cohort study examining birth outcomes in women with IBD demonstrated that the highest risks for preterm birth, low birth weight, and SGA infants were among women with active disease during pregnancy.[10] An elevated risk of preterm birth with higher inflammatory disease activity was replicated in a Danish cohort study of 163 births by 111 women with Crohn's disease (CD).[11] For these reasons, it is recommended that pregnant women with IBD are followed closely by a multidisciplinary care team, including a gastroenterologist who specializes in the care of IBD patients and a maternal-fetal medicine (MFM) specialist.[2]

The advent of biologic therapy, beginning with infliximab approval in 1998 for CD, has revolutionized the approach to treating patients with IBD. Increasing evidence has demonstrated the benefit of early introduction of biologic therapy to induce remission and reduce irreversible bowel injury.[12] There is a wealth of evidence to suggest that biologic therapy is safe in pregnancy, with equivalent risks of adverse pregnancy outcomes in IBD pregnancies with or without exposure to biologic therapy.[13,14] One notable prospective study of 1491 women with IBD found that drug exposure to biologics did not affect the rate of spontaneous abortions, congenital malformations, preterm birth, low birth weight, or infections in the first year of life.[15]

Given the increasing adoption of biologic therapies for IBD, including during pregnancy, we hypothesize that adverse obstetric and fetal outcomes have declined over time. Current research on evolving obstetric and fetal outcomes over the years, particularly in the era of biologic therapy, is limited. We thus aimed to examine trends in obstetric and fetal outcomes in pregnant patients with IBD and to compare the risks of these outcomes in IBD and non-IBD patients over a 20-year period.

Materials and Methods

Study Population and Data Collection

Data utilized for this study were obtained from the National Inpatient Sample (NIS), the largest publicly available all-payer inpatient healthcare database in the United States created for the Healthcare Cost and Utilization Project (HCUP).[16] The NIS contains data from more than 7 million hospital stays annually from 1998 onwards and represents approximately 20% of all discharges from nonfederal, short-term, and acute care hospitals across the country.

All obstetric hospitalizations involving a live delivery, stillbirth, or spontaneous abortion between 1998 and 2018 were identified using International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) codes from 1998 to 2015 and International Classification of Diseases, 10th revision and Clinical Modification/Procedure Coding System (ICD-10-CM/PCS) codes from October 2015 to 2018 (Supplemental Table 1). The ICD codes in any diagnosis position were also used to identify admissions with a diagnosis of CD or UC. The remainder of obstetric hospitalizations without a diagnosis of CD or UC were considered the comparison group.

Potential Confounders and Outcomes

Demographic variables extracted from the NIS included age, race, local median income (based on home zip code), and payer. Clinical variables included tobacco use, alcohol use, drug use, and presence of diabetes mellitus. We used the Deyo modification of the Charlson comorbidity index in our model, as higher scores are significantly associated with in-hospital complications, longer length of stay, and postoperative mortality.[12] Data on hospital-specific variables included hospital type and hospital size. Hospital type was divided into 3 categories by setting and teaching status: rural, urban nonteaching, and urban teaching. Hospital size was divided into 3 categories defined by relative number of beds: small, medium, and large.

Obstetric and fetal outcomes of interest for all IBD and non-IBD obstetric hospitalizations were identified via ICD-9-CM and ICD-10-CM/PCS codes in any position (Supplemental Table 1). Obstetric outcomes of interest included cesarean delivery, gestational diabetes, preeclampsia/eclampsia, PROM (defined as less than 24 hours before labor), and preterm delivery (defined as less than 37 weeks). Fetal outcomes of interest included fetal growth restriction (FGR), fetal distress, stillbirth, and spontaneous abortion. Fetal growth restriction, which is defined as infants who do not achieve full in utero growth potential, was selected instead of SGA as a more specific fetal outcome of interest, since SGA encompasses all infants born at a weight less than the 10th percentile due to FGR or normal factors (ie, maternal weight, maternal height).

Statistical Analysis

All data were analyzed using survey procedures that accounted for the complex sampling design of the NIS. Sampling weights provided from the NIS generally permit calculation of national estimates and require at least 1 observation per sampled hospital to be included for correct variance estimation. In the NIS redesign in 2012, the methodology for sampling was adjusted, thus affecting the weights. To provide consistency in weighted estimates across time in trend analyses, sampling weights for 1998 to 2011 were adjusted by HCUP; these weights were used in both cross-sectional and trend analyses. The proportion of live deliveries per 10 000 total deliveries was calculated for CD and UC patients for each year of the study period. The proportion of each outcome of interest per 100 total CD, UC, and non-IBD deliveries, respectively, was calculated for each year of the study period. Temporal trends were analyzed as change in proportion of each outcome of

Table 1. Demographic characteristics of the study cohort

	CD *n* = 48 986		UC *n* = 30 998		Non-IBD *n* = 69 963 805	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age	29.95	0.07	30.85	0.08	28.09	0.04
	n	**%**	**n**	**%**	**n**	**%**
Age group						
<20	1921	3.9%	858	2.8%	7395310	10.6%
20-30	24110	49.2%	13424	43.3%	37935223	54.2%
30-40	21945	44.8%	15850	51.1%	23333417	33.4%
40-50	1005	2.1%	848	2.7%	1294357	1.9%
50-60	5	0.0%	19	0.1%	5499	0.0%
Race						
White	33439	83.1%	21006	80.9%	30281387	53.9%
Black	3822	9.5%	1574	6.1%	7751542	13.8%
Other	2961	7.4%	3393	13.1%	18177057	32.3%
Charlson-Deyo comorbidity index						
zero	44246	90.3%	28373	91.5%	67326015	96.2%
1 to 2	4682	9.6%	2601	8.4%	2603707	3.7%
> 2	58	0.1%	25	0.1%	34083	0.0%
Tobacco use						
No	45556	93.0%	30333	97.9%	67095533	95.9%
Yes	3430	7.0%	665	2.1%	2868272	4.1%
Alcohol use						
No	48905	99.8%	30964	99.9%	69881440	99.9%
Yes	81	0.2%	34	0.1%	82365	0.1%
Drug use						
No	47826	97.6%	30705	99.1%	68987601	98.6%
Yes	1160	2.4%	294	0.9%	976205	1.4%
Diabetes						
No	48675	99.4%	30786	99.3%	69464515	99.3%
Yes	312	0.6%	212	0.7%	499290	0.7%
Local median income						
Quartile 1 (low)	7120	17.3%	3614	13.8%	13423991	26.9%
Quartile 2	9454	23.0%	5239	20.0%	12540507	25.2%
Quartile 3	11818	28.8%	7338	28.0%	12281775	24.6%
Quartile 4 (high)	12674	30.9%	9987	38.2%	11600819	23.3%
Payer						
Medicare	1287	2.6%	277	0.9%	389181	0.6%
Medicaid	10437	21.3%	4694	15.2%	27492563	39.4%
Private, HMO	35170	71.9%	24850	80.3%	37710448	54.0%
Other	2027	4.1%	1124	3.6%	4227760	6.1%
Hospital size						
Small	5822	11.9%	3732	12.1%	8596103	12.3%
Medium	12061	24.7%	7264	23.5%	19110723	27.4%
Large	30940	63.4%	19931	64.4%	42010108	60.3%
Hospital type						
Rural	4417	9.0%	2052	6.6%	8097790	11.6%
Urban, non-teach	14073	28.8%	8702	28.1%	26912325	38.6%
Urban, teach	30332	62.1%	20173	65.2%	34706819	49.8%
Hospital region						
Northeast	11413	23.3%	7781	25.1%	11942286	17.1%
Midwest	13974	28.5%	7613	24.6%	15199550	21.7%

Table 1. Continued

	n	%	n	%	n	%
South	16761	34.2%	9329	30.1%	26088625	37.3%
West	6838	14.0%	6274	20.2%	16733343	23.9%

interest in women with CD, UC, or no IBD across the 21 years. Additionally, odds ratios for each outcome were calculated over time for UC and CD patients compared with patients without IBD. For this analysis, years were grouped into quintiles (1998-2001; 2002-2005; 2006-2009; 2010-2013; 2014-2018) to account for stochastic changes from year to year and to facilitate the computational analysis. Absolute numbers were relatively small and similar across the 3 groups for the fetal outcomes of stillbirth and spontaneous abortion; thus temporal trends were not analyzed for these outcomes. Continuous variables were compared using the Student *t* test, and categorical variables were compared using the Pearson χ^2 statistic with second-order Scott-Rao modification. Multivariable logistic regression was performed to determine the adjusted odds ratio (aOR) for each outcome for pregnant women with CD and UC (compared with non-IBD), while adjusting for age, sex, race, tobacco use, alcohol abuse, drug use, diabetes mellitus, Charlson-Deyo comorbidity index, local median income, payer, hospital size, and hospital type. Due to multiple comparisons and very large sample size, statistical significance was defined as a 2-tailed $P < 0.001$. All statistical analyses were performed using SAS 9.4 (Cary, North Carolina).

Results

Demographic Characteristics

This study included 48 986 patients with CD (mean age 29.95 years, standard deviation [SD] 0.07), 30 998 patients with UC (mean age 30.85 years, SD 0.08), and 69 963 805 patients without IBD (mean age 28.06 years, SD 0.04). Demographic characteristics of the study cohort (patients and hospitals included) are shown in Table 1. Between 81% to 83% of IBD patients and 54% of non-IBD patients were white. The majority of IBD and non-IBD patients had a private or health maintenance organization (HMO) insurance payer. The distribution of median income quartile was essentially even amongst IBD and non-IBD patients. Greater than 90% of both IBD and non-IBD patients had no medical comorbidities (Charlson-Deyo comorbidity index of zero) and did not use tobacco, alcohol, or recreational drugs. Less than 1% of both IBD and non-IBD patients had a preexisting history of diabetes mellitus. The majority (63.4% of CD, 64.4% of UC, and 60.3% of non-IBD) of all patients delivered in large hospitals. While the majority of IBD patients (62.1% of CD and 65.2% of UC) delivered in urban teaching hospitals, just under half (49.8%) of non-IBD patients delivered in urban teaching hospitals (Table 1).

Trends in Obstetric and Fetal Outcomes Among All Patients

Among live deliveries, the proportion of mothers with IBD increased during the 20-year period (Figure 1). Crohn's disease deliveries increased from approximately 3.3 per 10 000 total deliveries in 1998 to 12.9 per 10 000 in 2018 ($P < 0.001$), and UC deliveries increased from approximately 2.3 per 10 000 in 1998 to 8.6 per 10 000 in 2018 ($P < 0.001$). Non-IBD deliveries decreased slightly, from 9994 per 10 000 total deliveries in 1998 to 9978 per 10 000 in 2018 ($P < 0.001$). The percentage of cesarean deliveries and deliveries complicated by gestational diabetes, preeclampsia/eclampsia, PROM, FGR, and fetal distress increased over time for both IBD and non-IBD women (Figure 2), while preterm deliveries decreased for both ($P < 0.001$) (Figure 3). Trends in stillbirth were not examined due to small absolute numbers, which were relatively similar across diagnoses and years.

IBD and Risk of Obstetric and Fetal Outcomes: Multivariable Analysis

In multivariable regression analyses, patients with CD and UC had a higher risk of cesarean delivery (CD aOR, 1.64; 95% confidence interval [CI], 1.57-1.71; UC aOR, 1.33; 95% CI, 1.26-1.41), preeclampsia/eclampsia (CD aOR, 1.39; 95% CI, 1.28-1.51; UC aOR, 1.27; 95% CI, 1.13-1.42), PROM (CD aOR, 1.19; 95% CI, 1.09-1.30; UC aOR, 1.45; 95% CI, 1.32-1.60), and preterm delivery (CD aOR, 1.50; 95% CI, 1.39-1.61; UC aOR, 1.45; 95% CI, 1.31-1.60) compared with patients without IBD (Table 2). Regarding fetal outcomes of interest, IBD conferred a higher risk of FGR (CD aOR, 1.74; 95% CI, 1.56-1.94; UC aOR, 1.53; 95% CI, 1.32-1.77) compared with patients without IBD (Table 2). Patients with UC (but not CD) had a higher odds ratio of delivery complicated by fetal distress (aOR, 1.26; 95% CI, 1.17-1.34) compared with patients without IBD. Inflammatory bowel disease did not confer a higher risk of gestational diabetes or stillbirth in our study cohort. As spontaneous abortions particularly in the early trimesters are frequently experienced outside of the hospital and do not necessitate hospital admission, this outcome of interest was ultimately excluded to avoid misclassification or misrepresentation of risk.

IBD and Risk of Obstetric and Fetal Outcomes: Trends in Odds Ratios

In evaluating trends in odds ratios for each outcome of interest in IBD patients compared with patients without IBD, the odds ratio for preterm deliveries decreased over time in both CD (OR, 1.95 in 1998-2001 to OR 1.40 in 2014-2018) and UC (OR, 2.01; 95% CI, 1.64-2.47 in 1998-2001 to OR 1.15; 95% CI, 0.98-1.36 in 2014-2018). The odds ratio for cesarean delivery and FGR decreased over time for both CD and UC patients when compared with patients without IBD, remaining above 1 (Figure 4). The odds ratio for PROM decreased over time in CD patients when compared with patients non-IBD patients, remaining above 1. In UC patients, the odds ratio for PROM when compared with patients without IBD did not demonstrate a clear trend (Figure 4). The odds ratio for preeclampsia/eclampsia, gestational diabetes, and fetal distress did not demonstrate a statistically

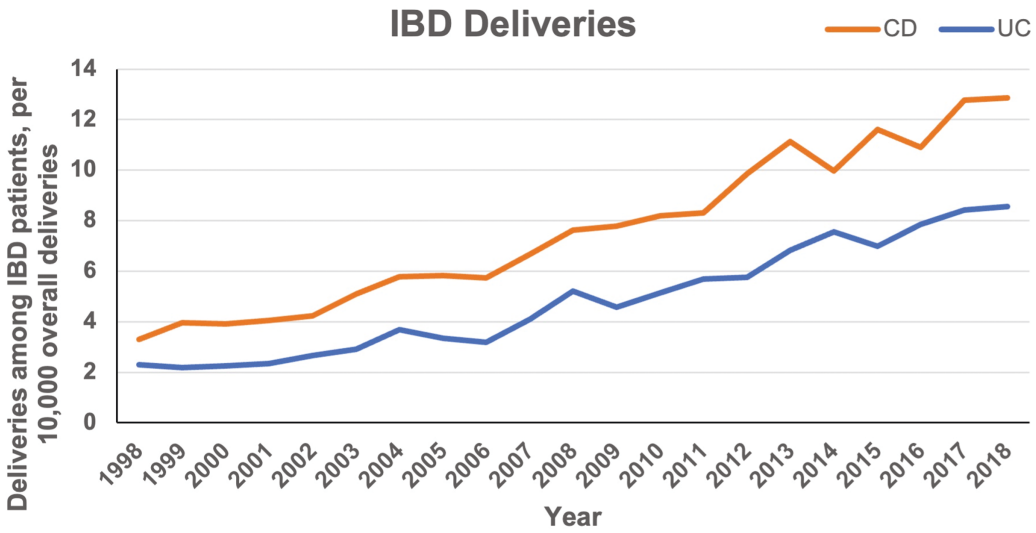

Figure 1. Proportion of overall deliveries among patients with inflammatory bowel disease between 1998 and 2018.

significant change over time in UC and CD patients when compared with patients without IBD (Supplemental Table 2).

Discussion

In this novel study of longitudinal obstetric and fetal outcomes over 20 years, the proportion of live deliveries from mothers with IBD increased steadily. For mothers with and without IBD, there was a general increase in cesarean deliveries, gestational diabetes, preeclampsia/eclampsia, PROM, FGR, and fetal distress, while preterm deliveries decreased. With the evolving landscape of IBD treatment, the odds ratios decreased over time for preterm delivery, cesarean delivery, and FGR in UC and CD patients and PROM in CD patients when compared with patients without IBD. However, IBD still confers a higher risk for many adverse obstetric and fetal outcomes. Though there have been prior studies examining obstetric and fetal outcomes in women with IBD, this study is unique in its examination of these outcomes longitudinally over a 20-year period.

We found that the proportion of live deliveries from mothers with a diagnosis of IBD increased from 1998 to 2018. This is most likely a reflection of the increase in IBD incidence in the western world (including North America, Australia, New Zealand, and western Europe) during the latter half of the 20th century.[17] Although the incidence of IBD reportedly stabilized and may have even decreased in North America at the turn of the 21st century, the estimated prevalence continues to rise.[18]

Trends in obstetric and fetal outcomes followed a similar pattern amongst IBD and non-IBD patients. In evaluating the downtrend of preterm deliveries over time, the rate of decline in patients with IBD appears more rapid than that of patients without IBD. Additionally, there was a decline in the odds ratio over time of preterm delivery in UC and CD patients compared with non-IBD patients. Corticosteroid use has been associated with preterm delivery amongst women with IBD.[19] The decline in preterm births in IBD patients may be related to the changing landscape of IBD therapy with the advent and increased use of steroid-sparing therapy as the mainstay of IBD management.

With the changing landscape of IBD therapy, our data demonstrate that there has been a relative decrease in the odds of certain adverse pregnancy outcomes in women with IBD. However, women with IBD overall continue to demonstrate increased risk of adverse obstetric and fetal outcomes. As noted in prior studies, disease activity has been defined as a preeminent risk factor for adverse obstetric and fetal outcomes amongst patients with IBD. Our data suggest that disease activity during pregnancy may still be an ongoing issue for women with IBD. This could be due to an underutilization of biologic therapy during pregnancy or the preconception period. Studies still show relatively lower use or delayed initiation of biologic therapy for IBD compared with nonbiologic therapies.[20] This may be partially due to barriers associated with biologic therapy, including the need for prior authorization, logistics surrounding method of drug delivery, and need for frequent drug monitoring.[20,21] Current guidelines recommend continuing biologic therapy during pregnancy, as the benefit of maintaining remission and avoiding flares outweighs any risk conferred by biologic therapy itself.[2,4] Despite what guidelines suggest, there may be ongoing hesitancy amongst women regarding biologic use during pregnancy. This has been highlighted in survey studies amongst women with other autoimmune conditions.[22] Women with IBD may undergo medication adjustments at the time of pregnancy due to concerns regarding teratogenic effects that ultimately result in increased disease activity. Given the use of a national administrative database for data collection, the treatment regimen and disease activity for each patient at the time of pregnancy was not known. As a result, further investigation would be needed to determine any definitive association between use of biologic therapy and trends in pregnancy outcomes for IBD patients over time. Alternatively, there may be other IBD-related factors aside from disease activity such as nutritional status that continue to elevate risk of adverse obstetric and fetal outcomes in IBD patients. To a lesser extent, a steady increase in adverse obstetric and fetal outcomes was also seen in women without IBD, suggesting that there are non-IBD related factors involved as well. This general rise in adverse pregnancy outcomes over time has been documented in prior studies and may be attributed to

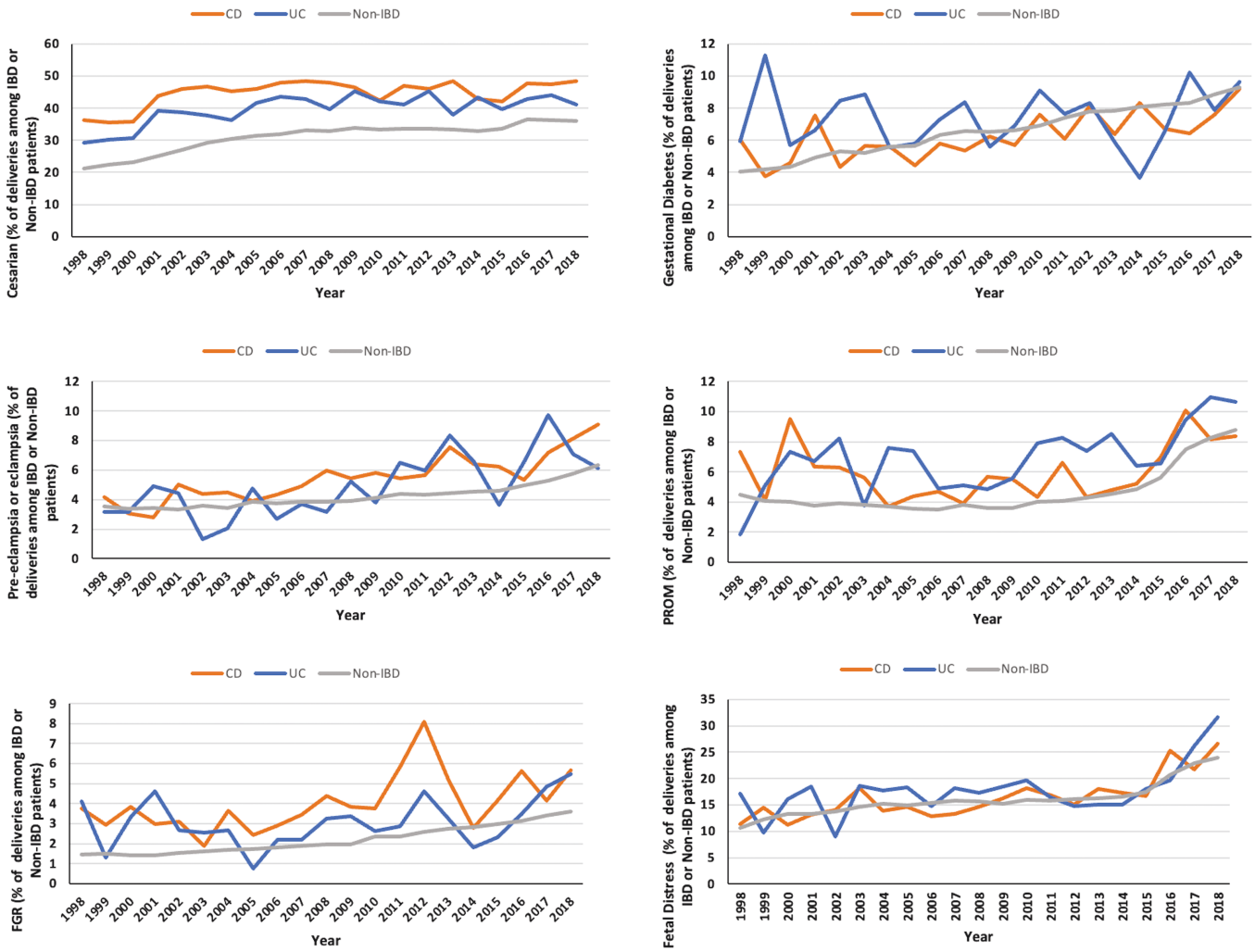

Figure 2. Trends in obstetric (cesarean delivery, gestational diabetes, preeclampsia, PROM), and fetal (fetal growth restriction, fetal distress) outcomes.

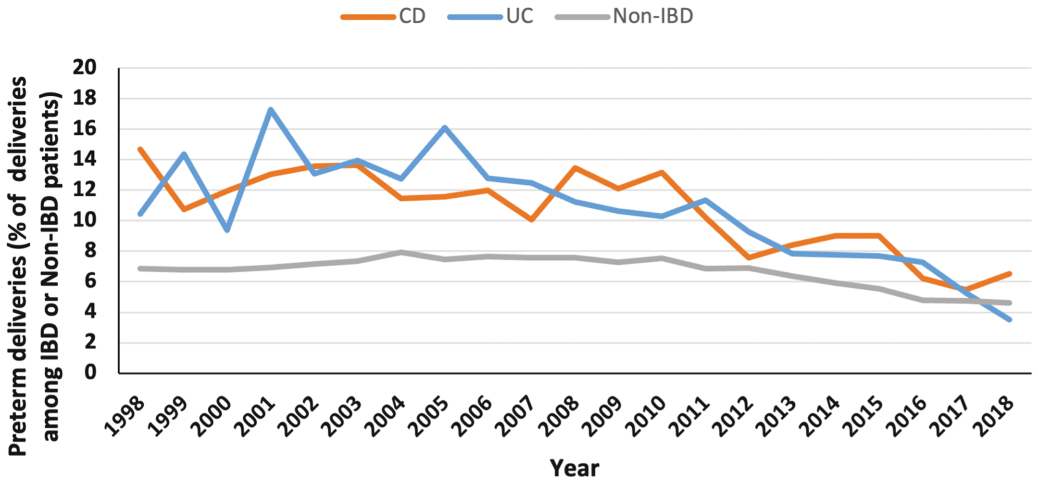

Figure 3. Trend in proportion of preterm deliveries for IBD and non-IBD patients, showing a decrease over time between 1998 and 2018.

an increase in preexisting conditions (such as obesity, insulin resistance, and hypertension) amongst women across the reproductive age spectrum prior to conception.[23]

There were limitations in our study. Our data were abstracted from an administrative data set, which inherently resulted in a lack of granular data on disease-specific characteristics related to our IBD study population, such as IBD phenotype, disease activity, and treatment courses. As a result, our data did not include disease activity at the time of pregnancy or use of biologics, as variables to allow for subgroup

analyses to assess if the risks demonstrated in IBD patients are ameliorated with reduced disease activity or with use of biologics. Nonetheless, this was an ecological study, and the primary objective was to investigate whether there were broad improvements in obstetric and fetal outcomes over time among women with IBD. This choice of data set allowed for a sufficiently large sample size to evaluate this objective. Given our data were abstracted from obstetric hospital admissions, we also were unable to fully characterize the risk and prevalence over time of spontaneous abortions in IBD and non-IBD patients, as this frequently occurs outside of the hospital. Additionally, our data did not include women who elect to proceed with home or out-of-hospital births, which make up approximately 1% to 2% of live births in the United States.[24] However, patients with IBD may be more likely to pursue in-hospital deliveries given their inherent medical complexity and need for specialty care.

Overall, trends in obstetric and fetal outcomes have followed a similar trajectory over time amongst patients with and without IBD. There has been an appreciable decrease in the odds of certain adverse pregnancy outcomes over time for patients with IBD potentially attributable to the advent and

Table 2. Multivariable analysis showing the adjusted odds ratio for each obstetric and fetal outcome in patients with inflammatory bowel disease

		CD		UC	
		aOR (95% CI)[a]	*P*	aOR (95% CI)[a]	*P*
Obstetric outcomes	Cesarean delivery	1.64 (1.57-1.71)	<0.001	1.33 (1.26-1.41)	<0.001
	Gestational diabetes	0.96 (0.87-1.05)	0.33	1.00 (0.90-1.11)	0.98
	Preeclampsia/eclampsia	1.39 (1.28-1.51)	<0.001	1.27 (1.13-1.42)	<0.001
	PROM	1.19 (1.09-1.30)	<0.001	1.45 (1.32-1.60)	<0.001
	Preterm delivery	1.50 (1.39-1.61)	<0.001	1.45 (1.31-1.60)	<0.001
Fetal outcomes	Stillbirth	1.04 (0.80-1.35)	0.77	1.50 (1.14-1.97)	0.004
	FGR	1.74 (1.56-1.94)	<0.001	1.53 (1.32-1.77)	<0.001
	Fetal distress	1.07 (1.01-1.13)	0.02	1.26 (1.17-1.34)	<0.001

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CD, Crohn's disease; FGR, fetal growth restriction; PROM, premature rupture of membranes; UC, ulcerative colitis.
[a]Adjusted for age, race, tobacco use, alcohol use, drug use, Charlson-Deyo comorbidity index, diabetes mellitus, median income quartile, payer, hospital size, hospital type.

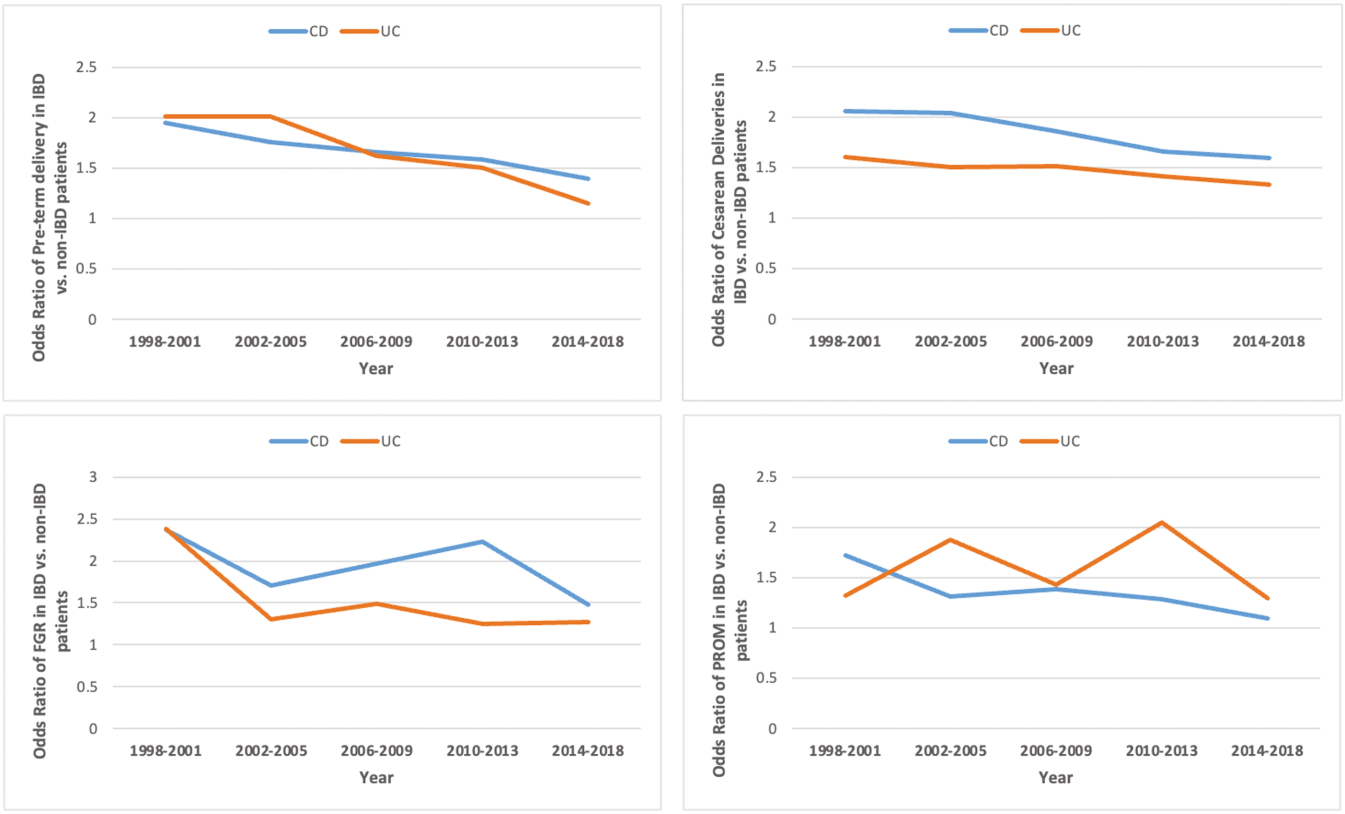

Figure 4. Trends in odds ratios for preterm delivery, cesarean delivery, fetal growth restriction, and PROM over time in CD and UC patients compared with non-IBD patients.

implementation of new therapies. However, IBD still confers demonstrable risk of adverse obstetric and fetal outcomes. Further investigation into factors to improve disease control (eg, medication adherence) and factors beyond disease activity that could elevate risk may elucidate strategies to mitigate adverse obstetric and fetal outcomes in pregnant patients with IBD.

Supplementary Data

Supplementary data is available at *Inflammatory Bowel Diseases* online.

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Conflicts of Interest

P.P., A.D., Y.B., A.P., and B.N.L. report no conflicts of interest. P.C. reports receiving funding from the National Institute of Diabetes and Digestive and Kidney Diseases outside the submitted work and serving as a Steering Committee member of the Alcohol-associated Liver Disease Special Interest Group and a Practice Guidelines Committee member for the American Association for the Study of Liver Diseases.

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