BJOG An International Journal of Obstetrics and Gynaecology

DOI: 10.1111/1471-0528.13946
www.bjog.org

Maternal medicine

Inflammatory bowel disease in pregnancy: a population-based study of prevalence and pregnancy outcomes

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Accepted 19 January 2016. Published Online 29 February 2016.

Objective To determine the prevalence of the inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease (CD), in pregnant women and determine pregnancy and fetal/neonatal outcomes.

Design Population-based cohort study.

Setting New South Wales, Australia, 2001–11.

Population A total of 630 742 women who delivered at ≥20 weeks of gestation.

Methods Descriptive and multivariate regression analyses of perinatal data linked to hospital admission data. We compared birth outcomes of women with and without a documented diagnosis of IBD.

Main outcome measures Caesarean section, severe maternal morbidity, preterm birth <37 weeks of gestation, planned preterm birth, small-for-gestational-age (birthweight <10th centile), perinatal mortality (stillbirth/neonatal death ≤28 days).

Results In all, 1960 women (0.31%) with IBD, who had 2781 births (1183 UC, 1287 CD and 311 IBD-indeterminate). Women with IBD were more likely than women without IBD to have a caesarean section [41.5 versus 28.2%, adjusted risk ratio (aRR) 1.38, 95% CI 1.31–1.45], severe maternal morbidity (2.6 versus 1.6%, aRR 1.54, 95% CI 1.17–2.03), preterm birth (9.7 versus 6.6%, aRR 1.47, 95% CI 1.30–1.66), planned preterm birth (5.3 versus 2.9%, aRR 1.74, 95% CI 1.47–2.07), and their infants to be small-for-gestational-age (9.7 versus 9.5%, aRR 1.19, 95% CI 1.04–1.36). There was no evidence of a difference in perinatal mortality.

Conclusion Pregnancy-associated IBD is more common than previously reported. Pregnancies complicated by IBD at or near the time of birth have significantly higher rates of adverse pregnancy outcomes than pregnancies of women without IBD.

Keywords Crohn's disease, inflammatory bowel disease, population-based, pregnancy, ulcerative colitis.

Tweetable abstract Increased rates preterm birth and caesarean section in women with inflammatory bowel disease.

Please cite this paper as: Shand AW, Chen JS, Selby W, Solomon M, Roberts CL. Inflammatory bowel disease in pregnancy: a population-based study of prevalence and pregnancy outcomes. BJOG 2016;123:1862–1870.

Introduction

The inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease (CD) are chronic inflammatory diseases that commonly affect people of childbearing age.[1]

The prevalence of IBD appears to be increasing worldwide, although the prevalence varies according to country and ethnicity.[2] The reasons for this are not known; however, IBD may be influenced by diet and genetic differences. Smoking is also associated with an increased risk of CD and with a worse course of CD.[1] A recent population-based study showed a high rate of IBD in Australia compared with other countries.[2,3]

Inflammatory bowel disease is treated with surgery and immune-modulating medications. Historically, women with

[†]Dr Jian Sheng (Charles) Chen died just after the completion of this project and we intend this work to be a tribute and a further example of the extraordinary contribution his work has made to the analysis of linked data.

IBD were advised that pregnancy was associated with adverse pregnancy outcomes, including preterm birth and small-for-gestational-age infants.[4] There has been improvement in medical treatments of IBD over time, including new biological treatments such as the anti tumour necrosis factor-α medications infliximab and adalimumab, which have become available for moderate and severe IBD. Rates of surgery for IBD have been reported to be decreasing.[5,6] Studies have also shown that women with active disease or previous abdominal surgery had reduced pregnancy rates.[7–9] A population-based study from Sweden showed that women with IBD had twice the rate of caesarean section compared with control women, and that women with UC had increased rates of venous thromboembolism (VTE).[10] A subsequent Swedish population-based study found that women with IBD had higher rates of preterm birth and low birthweight and that women with CD were at greater risk of stillbirth, particularly if they had active disease during pregnancy.[11]

The aim of our study was to determine the frequency of IBD in a contemporary population of pregnant women and to determine the maternal and fetal/neonatal outcomes of women with IBD.

Methods

The study population included all women who gave birth at ≥20 weeks of gestation in New South Wales (NSW), Australia during 2001–11. NSW is the most populous state of Australia with a resident population of approximately 7 million. Data were obtained from longitudinally linked population data sets for births: the NSW Perinatal Data Collection, (birth data) a population-based surveillance system of all births (≥20 weeks gestation or ≥400 g birthweight) linked to the NSW Admitted Patient Data Collection from July 2000 to December 2011 (hospital data) an administrative database of all public and private hospital admissions in NSW. The birth and hospital data sets were linked using probabilistic linkage methods and made available to the researchers as de-identified data.[12] Linkage proportions for maternal records is >98%.[13] Longitudinal linkage allows comprehensive assessment of pregnancy and non-pregnancy hospital admissions as well as birth history.[14]

Women with IBD (UC or CD) were identified from the hospital data, based on a diagnosis of IBD made in the medical records by an attending medical practitioner and subsequently coded in the medical record. More than 20 diagnoses and procedures for each hospital admission can be recorded, and are coded according to the International Classification of Disease Version 10 Australian Modification (ICD10AM)[15] and the Australian Classification for Health Interventions.[16] IBD could have appeared as the primary admitting diagnosis or as a comorbid condition for non-pregnancy, or pregnancy-related admissions. IBD was classified as UC or CD, or when women were recorded as having both UC and CD, the type of IBD was recorded as IBD-indeterminate.

The exposure of interest was an IBD diagnosis that could potentially affect pregnancy outcomes. In consultation with experts in the field, and the known risk of postpartum exacerbation, this was considered to be any hospitalisation before, during, or within the 6 months after the index birth where a diagnosis of UC or CD was recorded.[17] Births where the mother's first available record of diagnosis of IBD was >6 months after the birth were classified as no IBD at the time of birth.

Maternal outcomes included any caesarean section, prelabour caesarean section, induction of labour, instrumental delivery, third- or fourth-degree tear, episiotomy, gestational diabetes, pregnancy hypertension (gestational hypertension, pre-eclampsia and eclampsia), antepartum haemorrhage, postpartum haemorrhage, severe life-threatening maternal morbidity (e.g. organ failure, need for unanticipated surgical intervention),[18] thromboembolic events (puerperal deep vein thrombosis, pulmonary embolism or cerebral VTE up to 42 days postpartum), and pregnancy loss before 20 weeks of gestation (miscarriage/termination of pregnancy). Neonatal outcomes included preterm birth (<37 weeks gestation), spontaneous or planned (by prelabour caesarean or labour induction) preterm birth, small-for-gestational-age (10th centile for gestational age),[19] neonatal intensive care admission, severe neonatal morbidity (e.g. respiratory failure, mechanical ventilation, blood transfusion, sepsis),[20] Apgar score <7 at 5 min, major congenital anomaly[21] and stillbirth and neonatal death. Stillbirth is defined as a fetal death of at least 20 weeks gestation or 400 g birthweight. Neonatal death is defined as a death during the first 28 days or where the infant was never discharged home alive. Only factors that have previously been demonstrated to be reliably reported in the population health data were included in the analyses.[22–24] Health care utilisation included length of maternal hospital stay, number of antenatal admissions, tertiary obstetric hospital at birth, or postpartum hospital admission for any cause, gastrointestinal cause or postpartum VTE.

Other factors potentially predictive of adverse pregnancy outcomes were obtained from either or both of the data sets, including maternal age, parity, multiple pregnancy, artificial reproductive technology, maternal chronic hypertension, pregestational diabetes, morbid obesity, smoking during pregnancy, country of birth, socio-economic status (quintiles of the Australian Bureau of Statistics Index of

Relative Socio-economic Disadvantage calculated according to postcodes and weighted to the population in NSW)[25] and urban residence at delivery. Few records were missing data on these factors (<1%). The explanatory factors are reported with a high level of accuracy.

Statistical analyses

Descriptive statistics were used to summarise the distributions of maternal and pregnancy characteristics among all women with and without IBD and by IBD type. Multivariate models (including the covariate factors listed in Table 1) were used to determine the adjusted associations between IBD and study outcomes. Because many outcomes were common (>10%), and an odds ratio would not provide a good estimate of the relative risk, Poisson regression modelling with robust standard errors[26] was used for most maternal and neonatal outcomes. For some uncommon outcomes the 'modified Poisson' models failed to converge. In these instances, an adjusted odds ratios was calculated using a logistic regression model. For uncommon outcomes, the odds ratio provides a good estimate of the relative risk. The 95% CI were calculated for all effect estimates. A cluster effect was used to account for nonindependence in study outcomes for women with more than one pregnancy in the study. Deliveries with missing data (1.3%) on one or more risk factors were excluded from these analyses. The relationship between IBD and maternal factors and pregnancy outcomes was reported as crude and adjusted relative risk (RR and aRR) or crude or adjusted odds ratio with 95% CI. Results are reported for any IBD except where there were significant differences in findings for UC and CD. To determine the number of additional outcomes associated with IBD compared with those without IBD, we calculated the risk difference using the adjusted relative risk [(aRR − 1) × risk in deliveries to women without IBD × 100].[27] We also undertook a *post hoc* sensitivity analysis excluding the women with a first IBD admission in the 6 months postpartum.

Results

Among the 630 114 women who had 993 567 births, 2781 births were to 1960 women (0.31%) who had IBD recorded as a diagnosis either before the pregnancy, during the pregnancy or within 6 months postpartum. This included 1183 births where the mother had UC, 1287 births where the mother had CD, and 311 births where the mother's IBD was classified as IBD-indeterminate. Characteristics at birth for women by IBD classification are reported in Table 1. Women with IBD were older, more likely to have a birth after artificial reproductive technology, less likely to smoke during pregnancy, less likely to be born in Asia and were more likely to be socio-economically disadvantaged (all $P < 0.001$). Women with IBD were more likely to have a multiple pregnancy (twin or triplet or more) ($P < 0.01$) and more likely to have a termination of pregnancy or miscarriage ($P = 0.004$) than women without IBD. Women with CD were more likely to be smokers (13.3%) than women with UC (6.4%).

Maternal outcomes for women with IBD are reported in Table 2. Women with IBD were 38% more likely to have a caesarean section than women without IBD (aRR 1.38, 95% CI 1.31–1.45), 58% more likely to have a prelabour caesarean section (aRR 1.58, 95% CI 1.47–1.69) and 54% more likely to have severe maternal morbidity (aRR 1.54, 95% CI 1.17–2.03). Women with IBD had twice the rates of postpartum VTE compared with women without IBD (aRR 2.05, 95% CI 1.02–4.10). However, when stratified by mode of birth the risk of VTE was no longer statistically significant (aRR 1.88, 95% CI 0.94–3.77). With the exception of obstetric interventions, the absolute effect of IBD on pregnancy outcomes was <1 per 100 deliveries to women with IBD (Table 2). Women with IBD had longer lengths of hospital stay, more antenatal admissions and greater rates of postpartum gastrointestinal admissions (all $P < 0.001$). There was no evidence of difference in rates of pregnancy hypertension or gestational diabetes, antepartum haemorrhage or postpartum haemorrhage.

Neonatal outcomes for women with IBD are reported in Table 3. Women with IBD were 47% more likely to have an increase in preterm birth (aRR 1.47, 95% CI 1.30–1.66), compared with women without IBD, due to a 74% increase in planned preterm birth (aRR 1.74, 95% CI 1.47–2.07) and a 29% increase in spontaneous preterm birth (aRR 1.29, 95% CI 1.08–1.55). This was associated with a 10% increase in neonatal intensive care admission rates (aRR 1.10, 95% CI 1.02–1.19). There was a 20% increase in small-for-gestational-age (aRR 1.19, 95% CI 1.04–1.36). There was no evidence of difference in major congenital anomalies overall and there was no evidence of difference in perinatal death rates in women with IBD compared with women without IBD (0.8 versus 0.8%, aRR 1.0, 95% CI 0.66–1.51).

Compared with women with CD, women with UC were less likely to have a caesarean section (43.8 versus 38.0%, aRR 0.85, 95% CI 0.76–0.95, $P = 0.003$), and less likely to have a prelabour caesarean section (30.9 versus 25.4%, aRR 0.78, 95% CI 0.67–0.90, $P < 0.001$, Table 2), but were more likely to have an infant with major congenital anomalies (2.3 versus 4.4%, aRR 2.0, 95% CI 1.25–3.20, $P = 0.004$, Table 3). There were 1.2 additional major anomalies per 100 infants born to women with UC (Table 3). There was no evidence of differences between women with UC or CD. The findings remained unchanged when the 151 (5.4%) women who had a first IBD-related hospitalisation after birth were excluded.

Table 1. Characteristics and health service utilisation for births in New South Wales by IBD status

Maternal characteristics	No IBD (*n* = 990 786 births)	Any IBD (*n* = 2781 births)	Ulcerative colitis (*n* = 1183 births)	Crohn's disease (*n* = 1287 births)	IBD-indeterminate (*n* = 311 births)
Maternal age (year), median (interquartile range, IQR)	30.7 (26.6–34.4)	32.2 (28.9–35.3)	32.7 (29.4–35.6)	31.7 (28.3–34.9)	32.1 (29.2–35.1)
Nullipara, *n* (%)	416 717 (42.1)	1129 (40.6)	471 (39.8)	526 (40.9)	132 (42.4)
Number of births at last birth, mean (SD)	2.2 (1.2)	2.1 (1.1)	2.1 (1.1)	2.1 (1.0)	2.0 (1.0)
Multiple pregnancy, *n* (%)	15 409 (1.6)	64 (2.3)	25 (2.1)	32 (2.5)	7 (2.3)
Assisted reproductive technology birth, *n* (%)	22 332 (2.3)	111 (4.0)	46 (3.9)	51 (4.0)	14 (4.5)
Maternal hypertension, *n* (%)	6890 (0.7)	22 (0.8)	9 (0.8)	12 (0.9)	1 (0.3)
Termination/miscarriage over the study period, *n* (%)	105 144 (16.7)	384 (19.6)	157 (18.7)	178 (19.8)	49 (22.4)
Prepregnancy diabetes mellitus, *n* (%)	5647 (0.6)	17 (0.6)	10 (0.9)	4 (0.3)	3 (1.0)
Morbid obesity, *n* (%)	3133 (0.3)	5 (0.2)	4 (0.3)	1 (0.1)	0 (0)
Smoking during pregnancy, *n* (%)	135 270 (13.7)	278 (10.0)	76 (6.4)	171 (13.3)	31 (10.0)
Country of birth, *n* (%)*					
Australia/New Zealand	721 409 (72.8)	2378 (85.5)	991 (83.8)	1120 (87.0)	267 (85.9)
Europe, USA or Canada	61 818 (6.2)	186 (6.7)	79 (6.7)	83 (6.4)	24 (7.7)
Asia	127 268 (12.8)	73 (2.6)	48 (4.1)	21 (1.6)	4 (1.3)
Other	77 561 (7.8)	133 (4.8)	59 (5.0)	59 (4.6)	15 (4.8)
Socio-economic status, *n* (%)*					
Most disadvantaged	184 632 (18.6)	673 (24.2)	275 (23.2)	313 (24.3)	85 (27.3)
Disadvantaged	179 786 (18.1)	550 (19.8)	229 (19.4)	261 (20.3)	60 (19.3)
Average	204 290 (20.6)	571 (20.5)	246 (20.8)	272 (21.1)	53 (17.0)
Advantaged	196 079 (19.8)	495 (17.8)	219 (18.5)	224 (17.4)	52 (16.7)
Most advantaged	215 233 (21.7)	480 (17.3)	210 (17.8)	209 (16.2)	61 (19.6)
Health service utilisations					
Length of maternal hospital stay (days)					
Mean (SD)	4.9 (5.0)	5.5 (3.5)	5.4 (3.3)	5.6 (3.5)	5.8 (4.2)
Median (interquartile range)	5 (3–6)	5 (4–6)	5 (4–6)	5 (4–6)	5 (4–7)
No. of antenatal admissions, *n* (%)*					
0	704 447 (71.1)	1585 (57.0)	721 (61.0)	706 (54.9)	158 (50.8)
1	181 092 (18.3)	681 (24.5)	278 (23.5)	328 (25.5)	75 (24.1)
2–3	86 799 (8.8)	391 (14.1)	145 (12.3)	195 (15.2)	51 (16.4)
≥4	18 448 (1.9)	124 (4.5)	39 (3.3)	58 (4.5)	27 (8.7)
Tertiary obstetric care hospital at birth, *n* (%)	446 304 (45.1)	1103 (39.7)	439 (37.1)	531 (41.3)	133 (42.8)
Postpartum hospital admission, any cause, *n* (%)	104 271 (10.5)	775 (27.9)	323 (27.3)	332 (25.8)	120 (38.6)
Postpartum hospital admission, gastrointestinal cause, *n* (%)	4358 (0.4)	439 (15.8)	173 (14.6)	179 (13.9)	87 (28.0)
Postpartum venous thromboembolism, *n* (%)	1349 (0.1)	8 (0.3)	4 (0.3)	3 (0.2)	1 (0.3)

*Percentages do not add to 100%, due to missing data.

Discussion

Main findings

In this large population-based study of recent births with contemporary care, women with IBD had higher absolute and relative risks of caesarean section and preterm birth, than women without IBD; however, there was no increase in the rate of perinatal death, or severe neonatal morbidity in their infants. This study provides information to women with IBD that if they do conceive, perinatal outcomes are generally good. However, women with IBD were more likely to have a birth after artificial reproductive

Table 2. Relative risks and risk difference of maternal and pregnancy outcomes for births to women with IBD

Outcome variable	Risk factor	Outcome, *n* (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*	Risk difference (95% CI)**
Pregnancy hypertension	IBD	266 (9.6)	1.06 (0.93–1.20)	0.97 (0.86–1.10)	−0.3 (−1.3 to 0.9)
	No IBD	89 182 (9.0)	1.00	1.00	
Gestational diabetes	IBD	142 (5.1)	0.89 (0.75–1.05)	1.03 (0.87–1.23)	0.2 (−0.8 to 1.3)
	No IBD	57 225 (5.8)	1.00	1.00	
Antepartum haemorrhage	IBD	92 (3.3)	1.09 (0.89–1.34)	1.12 (0.91–1.38)	0.4 (−0.3 to 1.1)
	No IBD	30 118 (3.0)	1.00	1.00	
Induction of labour***	IBD	720 (36.2)	1.18 (1.11–1.26)	1.12 (1.05–1.19)	4.3 (1.8 to 6.9)
	No IBD	251 044 (30.2)	1.00	1.00	
Any caesarean section	IBD	1155 (41.5)	1.52 (1.38–1.67)	1.38 (1.31–1.45)	10.7 (8.7 to 12.7)
	UC	449 (38.0)	1.55 (1.35–1.77)	1.42 (1.24–1.63)	11.8 (6.8 to 17.8)
	CD	564 (43.8)	1.90 (1.67–2.16)	1.86 (1.63–2.12)	24.3 (17.8 to 31.6)
	No IBD	279 662 (28.2)	1.00	1.00	
Prelabour caesarean section	IBD	792 (28.5)	1.71 (1.58–1.86)	1.58 (1.47–1.69)	9.4 (7.6 to 11.2)
	UC	300 (25.4)	1.77 (1.52–2.05)	1.54 (1.32–1.79)	8.8 (5.2 to 12.8)
	CD	398 (30.9)	2.28 (1.99–2.62)	2.18 (1.89–2.53)	19.1 (14.4 to 24.8)
	No IBD	160 715 (16.2)	1.00	1.00	
Instrumental delivery****	IBD	243 (14.9)	1.11 (0.98–1.24)	1.09 (0.97–1.22)	1.2 (−0.4 to 3.0)
	No IBD	95 068 (13.4)	1.00	1.00	
Third- or fourth-degree tear****	IBD	37 (2.3)	0.87 (0.63–1.21)	0.96 (0.69–1.33)	−0.7 (−5.4 to 5.7)
	No IBD	18 331 (2.6)	1.00	1.00	
Episiotomy****	IBD	281 (17.3)	1.04 (0.93–1.17)	1.11 (1.00–1.24)	1.8 (0.0 to 3.8)
	No IBD	113 848 (16.0)	1.00	1.00	
Postpartum haemorrhage	IBD	241 (8.7)	0.90 (0.73– 1.13)	0.99 (0.87–1.14)	−0.1 (−1.1 to 1.2)
	No IBD	86 358 (8.7)	1.00	1.00	
Severe maternal morbidity	IBD	72 (2.6)	1.38 (1.03–1.85)	1.54 (1.17–2.03)	0.9 (0.3 to 1.7)
	No IBD	15 948 (1.6)	1.00	1.00	
Postpartum VTE	IBD	8 (0.3)	2.14 (1.07–4.28)	2.05 (1.02–4.10)	0.1 (0.0 to 0.3)
	NO IBD	1349 (0.1)	1.00	1.00	
Any postpartum hospital admission	IBD	775 (27.9)	2.65 (2.49–2.82)	2.56 (2.40–2.73)	16.4 (14.7 to 18.2)
	NO IBD	104 271 (10.5)	1.00	1.00	
Postpartum hospital admission—gastrointestinal cause	IBD	439 (15.8)	36.1 (32.9–39.7)	36.2 (32.9–39.8)	14.1 (12.8 to 15.5)
	NO IBD	4358 (0.4)	1.00	1.00	

*Adjusted for maternal age, country of birth, socio-economic status, urban or rural residence, chronic hypertension, pregestational diabetes, smoking during pregnancy, parity and multiple pregnancies.
**Number of additional outcomes per 100 births to women with IBD compared to those without.
***Excludes prelabour caesarean births.
****Among vaginal births.

technology, have higher rates of hospital admissions, longer stays in hospital and an absolute increased risk of 0.9% for severe maternal morbidity compared with women without IBD. The prevalence of IBD in women giving birth in NSW was higher (312 per 100 000) than reported in a recent study of women giving birth in California (130 per 100 000).[28] Rates of IBD have been found to be increasing worldwide, and some of the highest rates of IBD have been found in Australia.[1,2]

Strengths and limitations

The strength of the study is the large longitudinally linked population-based data set with recent data. Diagnoses and procedures are reliably reported in the hospital data set,[29] and the birth data are reliably reported. One of the limitations is that the prevalence of IBD may be an underestimate, due to women with relatively mild disease not requiring hospital admission, and hence women with more severe disease may have been over-represented in this study. In addition, the actual time of the diagnosis of the IBD was not known, only the date of the first hospital admission where a diagnosis was recorded. Another limitation of the study is that no information is available on pharmacological treatments, including the new biological treatments, nor how outcomes changed over time. Women may have variable compliance with their medication,

Table 3. Relative risks and risk difference of pregnancy and neonatal outcomes for women with IBD

Outcome variable	Risk factor	Outcome, *n* (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*	Risk difference*,**
Preterm birth (<37 weeks)	IBD	269 (9.7)	1.52 (1.35–1.72)	1.47 (1.30–1.66)	3.1 (2.0 to 4.4)
	No IBD	65 092 (6.6)	1.00	1.00	
Spontaneous preterm birth (<37 weeks)***	IBD	128 (4.9)	1.26 (1.05–1.52)	1.29 (1.08–1.55)	1.1 (0.3 to 2.2)
	No IBD	37 448 (3.9)	1.00	1.00	
Planned preterm birth (<37 weeks)***	IBD	141 (5.3)	1.85 (1.56–2.19)	1.74 (1.47–2.07)	2.2 (1.4 to 3.1)
	No IBD	27 644 (2.9)	1.00	1.00	
Small for gestational age (<10th centile)****	IBD	270 (9.7)	1.02 (0.90–1.17)	1.19 (1.04–1.36)	1.8 (0.4 to 3.4)
	No IBD	93 647 (9.5)	1.00	1.00	
Severe neonatal morbidity	IBD	145 (5.2)	1.17 (0.99–1.37)	0.94 (0.82–1.09)	−0.3 (−0.8 to 0.4)
	No IBD	44 436 (4.5)	1.00	1.00	
Apgar score at 5 minutes <7	IBD	42 (1.5)	1.10 (0.81–1.49)	1.03 (0.76–1.40)	0.0 (0.3 to 0.6)
	No IBD	13 695 (1.4)	1.00	1.00	
Admission neonatal intensive care (>4 hours)	IBD	504 (18.1)	1.19 (1.10–1.29)	1.10 (1.02–1.19)	1.5 (0.3 to 2.9)
	No IBD	150 476 (15.2)	1.00	1.00	
Stillbirth/neonatal death	IBD	22 (0.8)	0.95 (0.63–1.44)	1.00 (0.66–1.51)	0.0 (−0.3 to 0.4)
	No IBD	8286 (0.8)	1.00	1.00	
Major congenital anomalies****	IBD	90 (3.2)	1.02 (0.83–1.26)	1.00 (0.81–1.23)	0.0 (−0.6 to 0.7)
	UC	52 (4.4)	1.41 (1.06–1.86)	1.38 (1.04–1.82)	1.2 (0.1 to 2.6)
	CD	29 (2.3)	0.70 (0.48–1.03)	0.69 (0.47–1.00)	−1.0 (−1.7 to 0.0)
	No IBD	31 358 (3.2)	*1.00	*1.00	

*Adjusted for maternal age, country of birth, socio-economic status, urban or rural residence, any hypertension, any diabetes, smoking during pregnancy, parity and multiple pregnancy. Additional adjustment for preterm birth was applied to severe neonatal morbidity, Apgar score at 5 minutes (<7) and admission to neonatal intensive care unit.
**Number of additional outcomes per 100 infants born to women with IBD compared with those without.
***Compared with births at term.
****No convergence of general estimating equation parameter estimates after 50 iterations in a 'modified Poisson' approach suggested by Zou. Odds ratio was reported instead.

especially if they are worried about fetal effects. European guidelines state that medical treatment for IBD except methotrexate, should generally continue during pregnancy.[9]

A further limitation is that no information was available on disease activity, or other patient-level data such as body mass index, reasons for planned preterm birth or planned caesarean section. Women with IBD may experience a flare during or after pregnancy; a recent meta-analysis has found that women with IBD who conceive when their disease is active are more likely to have active disease during pregnancy than those who conceive when in remission.[30] An association with increased disease activity in CD and preterm birth has previously been reported[31] as has an association between UC and preterm birth, and between CD and stillbirth and particularly when there were flares throughout pregnancy.[11] There is slight uncertainty regarding the inclusion of women with the first record of IBD diagnosis after birth in the study. There were 151 (5.4%) women with a first record of IBD in the 6 months after delivery. However, even after excluding these women, there was no evidence of a difference in the overall results.

Interpretation

We found increases in the relative (RR = 1.47) and absolute (risk difference = 3.1) risk of preterm birth (primarily due to planned early delivery) in women with IBD. A review of studies that included a mixture of retrospective and prospective studies from a number of countries in Europe, Scandinavia and Israel from 1986 to 2012, found the relative risk of preterm birth in women with IBD ranged from 1.0 to 2.73.[32] However, whether the preterm birth was iatrogenic or spontaneous, the reason for preterm birth was not reported. This differed from the earlier meta-analysis published in 2007 that reported increased risks of preterm birth (OR 1.87, 95% CI 1.52–2.31, $P < 0.001$) and also increased risk of caesarean section in women with IBD (OR 1.51, 95% CI 1.27–1.81, $P < 0.001$).[33] We found no absolute or relative increase in the risk of perinatal death, similar to the meta-analysis that found no difference in the rates of stillbirths in women with IBD,[33] which was different from the large Swedish study that found that women with CD had an increased risk of stillbirth.[11] This highlights the difficulty of comparing studies from different

time periods and countries, as women may have had different disease management before or during pregnancy, which may explain the differences in outcomes.

Other studies have reported increased rates of VTE in men, and in pregnant and nonpregnant women with IBD.[10,34] Although we found a trend to increased rates of postpartum VTE in women with IBD and pregnancy, this was no longer significant after adjusting for mode of birth. The rate was lower than reported in a large population-based study from the USA using hospitalisation data from 2005, which showed women with IBD had a six-fold increased risk of VTE in pregnancy (risk of VTE in CD versus the non-IBD population: aOR 6.12; 95% CI 2.91–12.9), as well as increased risks of caesarean section, antenatal hospitalisations and blood transfusion.[35] There has been a lack of international consensus guidelines for prophylaxis of VTE in pregnant and postpartum women.[36] The type and uptake of VTE prophylaxis in women in this study is not known.

Women with IBD had high rates of postpartum admission for gastrointestinal indications. The impact of pregnancy on IBD is not completely known. It may be that women have delayed investigations or stopped treatment either during pregnancy or lactation, resulting in postpartum admission for gastrointestinal indications. However, it cannot be concluded that pregnancy was associated with a worsening of IBD. A population-based study from the USA has found that pregnancy in women with CD is a risk factor for complications requiring surgical intervention, in particular anorectal suppuration and intestinal genitourinary fistulae.[37]

This study showed that women with IBD had more socio-economic disadvantage, despite being older and smoking less. Having IBD is reported to impair work and educational performance, and this effect of the disease may reflect the difference in socio-economic status seen in women with IBD in this study.[38] Low socio-economic status has previously been reported to be associated with adverse health outcomes.

It has previously been found that women with IBD were concerned that IBD medication was harmful to their unborn children, and hence would consider stopping medication and putting up with symptoms.[39] They were also concerned that IBD could be passed onto their offspring, worried about infertility, and many had considered avoiding pregnancy because of their disease. A number of review articles and guidelines summarising the treatment recommendations for IBD in pregnancy and lactation have recently been published, and recommend that women plan pregnancy when in remission.[6,7,40] Education of women with IBD of childbearing age may include the provision of information about medications and nutrition (including prepregnancy folic acid), potentially changing medication to avoid teratogenicity, and possibly effective contraception to plan pregnancies when IBD is in remission.[41]

The standard indications for a caesarean section for women with IBD, aside from obstetric indications, are active perianal disease and previous pouch surgery; however, there may be significant variation between clinicians in recommendations of care for women of reproductive age with UC and an ileo-pouch anastomosis.[42] An association between birth by caesarean section and an increase in subsequent development of IBD particularly in childhood and young adulthood, has previously been reported,[43] so caesarean section for nonobstetric or non-gastrointestinal indications should be carefully considered. Multidisciplinary discussion involving colorectal surgery, gastroenterology and obstetrics to determine the optimal mode of birth for an individual woman is recommended.

Conclusions

Women with IBD have increased risks of adverse pregnancy outcomes including caesarean section and preterm birth. Although perinatal outcomes of women with IBD are generally good, women with IBD should be provided with information to optimise pregnancy outcomes and plan pregnancies when disease is stable.

Disclosure of interests

Full disclosure of interests available to view online as supporting information.

Contribution to authorship

AS and CR conceived the study. All authors contributed substantially to the design of the study, planning of data analysis, interpretation of results, and revised the article for intellectual content. AS drafted and revised the article. CR helped draft the article and provided clinical expertise. WS and MS provided clinical expertise and a critical review of the article. JSC performed the analyses of data, was involved in drafting the article and approved a near final version of the manuscript. All other authors read and approved a final version of the manuscript.

Details of ethics approval

The NSW Population and Health Services Research Ethics Committee approved the study. Approval number 2012-12-430. Date of approval 12.8.2013.

Funding

This study was funded by a research grant from the Society of Obstetric Medicine of Australia and New Zealand (SOMANZ). It was also supported by an Australian National Health and Medical Research Council (NHMRC)

Centre for Research Excellence Grant (1001066). CLR is supported by an NHMRC Senior Research Fellowship (#APP1021025).

Acknowledgements

We thank the New South Wales (NSW) Ministry of Health for access to the population health data and the NSW Centre for Health Record Linkage for linking the data sets. ■

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