

# Impact of the coronavirus infectious disease (COVID-19) pandemic on the provision of inflammatory bowel disease (IBD) antenatal care and outcomes of pregnancies in women with IBD

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## ABSTRACT

**Background** The impact of COVID-19 on pregnant inflammatory bowel disease (IBD) patients is currently unknown. Reconfiguration of services during the pandemic may negatively affect medical and obstetric care. We aimed to examine the impacts on IBD antenatal care and pregnancy outcomes.

**Methods** Retrospective data were recorded in consecutive patients attending for IBD antenatal care including outpatient appointments, infusion unit visits and advice line encounters.

**Results** We included 244 pregnant women with IBD, of which 75 (30.7%) were on biologics in whom the treatment was stopped in 29.3% at a median 28 weeks gestation. In addition, 9% of patients were on corticosteroids and 21.5% continued on thiopurines. The care provided during 460 patient encounters was not affected by the pandemic in 94.1% but 68.2% were performed via telephone (compared with 3% pre-pandemic practice;  $p < 0.0001$ ). One-hundred-ten women delivered 111 alive babies (mean 38.2 weeks gestation, mean birth weight 3324 g) with 12 (11.0%) giving birth before week 37. Birth occurred by vaginal delivery in 72 (56.4%) and by caesarean section in 48 (43.6%) cases. Thirty-three were elective (12 for IBD indications) and 15 emergency caesarean sections. Breast feeding rates were low (38.6%). Among 244 pregnant women with IBD, 1 suspected COVID-19 infection was recorded.

**Conclusion** IBD antenatal care adjustments during the COVID-19 pandemic have not negatively affected patient care. Despite high levels of immunosuppression, only a single COVID-19 infection occurred. Adverse pregnancy outcomes were infrequent.

## INTRODUCTION

The initial wave of the Sars-cov-2 pandemic led to vast disruption of patients' lives and was also associated with significant morbidity and mortality.<sup>1</sup> Furthermore, it led to many

## Summary box

### What is already known about this subject?

- ▶ The COVID-19 pandemic has impacted the ability to provide care for patients with inflammatory bowel disease (IBD).
- ▶ Pregnant women with active IBD are at an increased risk of adverse pregnancy outcomes.
- ▶ Changes to IBD antenatal care could adversely impact maternal and fetal outcomes.

### What are the new findings?

- ▶ IBD antenatal care was mainly provided remotely during the COVID-19 pandemic.
- ▶ The medical care provided was not affected by the pandemic in 94%.
- ▶ Continuation rates for biologics in the third trimester were higher than expected.
- ▶ Levels of adverse maternal and fetal outcomes were low.

### How might it impact on clinical practice in the foreseeable future?

- ▶ Clinicians looking after pregnant women with IBD should aim to maintain routine standards of care during the pandemic.
- ▶ Women with IBD should be reassured that we have not found increased risk of adverse events in our cohort.

vulnerable patients shielding and avoiding hospitalisations in order to protect themselves from what they perceived as a risk. As all women are at an increased risk of viral respiratory infections during pregnancy,<sup>2</sup> there was concern that pregnancy may be an independent risk factor for both acquiring COVID-19 and higher severity of



the infection. In the UK, pregnant women in their third trimester were considered moderate risk and hence were advised to stay at home as much as possible and adhere to strict social distancing.<sup>3</sup>

Pregnant women do not appear to be at a higher risk of contracting COVID-19.<sup>4</sup> The PregCov-19 study of 11 000 patients found common symptoms of fever, cough with less frequent symptoms of dyspnoea, myalgia, loss of sense of taste and diarrhoea.<sup>5</sup> The third trimester of pregnancy was associated with increased risk of hospitalisation,<sup>6</sup> and women were five times more likely to be admitted to intensive care in their second half of pregnancy with COVID-19.<sup>7</sup>

Compared with women who were not pregnant, pregnant or recently pregnant women who acquired COVID-19 were more likely to need admission to intensive care (OR: 1.51, CI: 1.33 to 1.96) and require invasive ventilation (OR: 1.88, CI: 1.36 to 2.60).<sup>5</sup> COVID-19 infection has been associated with adverse pregnancy outcomes including a three times greater risk of preterm birth,<sup>5</sup> and a higher incidence of caesarean section with 50% attributed to maternal or fetal compromise.<sup>6</sup> To date, there seems to be no significant increase in congenital abnormalities following maternal COVID-19 infection.<sup>8</sup> An increased risk of stillbirth has been reported in a single-centre study during the pandemic (n=16, 9.31 per 1000 births) compared with prepandemic (n=4, 2.38 per 1000 births; p=0.01), but as others studies have not replicated this result, the findings should be interpreted with caution.<sup>9</sup>

Inflammatory bowel disease (IBD) is diagnosed in 50% of cases under the age of 35 and affects many women of childbearing age.<sup>10</sup> About 25% of women will conceive for the first time following their diagnosis of IBD.<sup>11</sup> Women of childbearing age with coexisting IBD should be counselled on fertility, efficacy of contraceptives, medications used to control IBD, teratogenicity and delivery methods.<sup>12</sup> Approximately, a third of patients in remission will relapse,<sup>13</sup> with almost two-thirds with active disease at conception having further flare ups during pregnancy.<sup>14,15</sup> This is especially important as active IBD is considered an independent risk factor for poorer outcomes from COVID-19 in general and hence optimal disease control during pregnancy is vital for both the pregnant woman and the foetus.<sup>16</sup> To date, the impact on IBD pregnancies during the COVID-19 pandemic remains to be established.

Service restructuring during the pandemic may also contribute to the impact of COVID-19 on pregnant patients with IBD. Patients may have experienced reductions in antenatal and postnatal appointments, reduced access to midwife led birth settings and alternative methods of screening for gestational diabetes and fetal growth restriction. There has also been an increase in telemedicine, virtual appointments and reduction in face-to-face appointments during the COVID-19 pandemic.<sup>17</sup>

We therefore aimed to investigate the impact on the provision of IBD antenatal care and pregnancy outcome of women with IBD during the COVID-19 pandemic in the UK.

## METHODS

The study captured routinely collected clinical data arising from IBD antenatal care. Consecutive patients attending for IBD antenatal care at 13 British hospitals (Wolverhampton, Newcastle, Leeds, Hull, Bristol Royal Infirmary, Liverpool, Bolton, King's College Hospital, Glasgow Royal Infirmary, St Georges, Barts and the London, Pennine Acute Hospitals and Sheffield) from March to August 2020 were recruited. All sites maintained a prospective patient register. Patients with a pregnancy of any gestational age were eligible but in many centres, joint obstetric IBD clinics only review patients after a 12-week scan demonstrating a viable pregnancy.

IBD clinicians collected data pro- and retrospectively on patients' demographics (age, ethnicity), disease phenotype, surgical history and treatment characteristics. In addition, the type of patient encounter (face-to-face IBD clinic, telephone IBD clinic, combined antenatal clinic face to face, combined antenatal clinic telephone, IBD advice-line encounter of patients contacting their IBD service by phone or email), change to appointment type due to the pandemic and tests requested for IBD were recorded. Clinicians recorded whether their practice diverged from their usual care due to effects from the pandemic (choice of medical treatments, diagnostics and follow-up). We recorded clinicians' decisions on whether they would opt for a different appointment type or clinical management had it not been during the pandemic. We did however not use a historic prepandemic control group of cases and appointments. Disease activity was measured by Physicians Global Assessment (PGA) and the worst disease activity during pregnancy was used for all analyses. For those women who gave birth during the study period, we recorded gestational age at birth, delivery method, infant's weight, sex and feeding status as well as maternal complications and congenital abnormalities.

The study was conducted as a pragmatic clinical audit and hence no sample size calculations were performed. Data were predominantly presented in descriptive manner. Analysis was performed using SPSS (V.22).  $\chi^2$  was used to establish difference between categorical variables. Significance was considered when p value was <0.05.

This project was considered a clinical audit service evaluation and hence formal ethical approval was not necessary.

## RESULTS

### Study cohort

A total of 244 women (mean age 31.3 years; 93.4% caucasian) were included (table 1). Of these, 110 (45.1%) had a diagnosis of Crohn's disease (CD), 124 (50.8%) ulcerative colitis (UC) and 10 (4.1%) were classed as IBD-unclassified (IBD-U). Further details on phenotype, parity and surgical treatment history are displayed in table 1. Data on worst disease activity during pregnancy as assessed by PGA were available for 232 women. Of these,

**Table 1** Patient characteristics, phenotype, parity and treatment history

	Number of patients	Percentage of patients
<b>Ethnicity</b>		
Caucasian	197	93.40
Mixed	1	0.50
Asian	1	0.50
Black	6	2.80
Other	6	2.80
Not stated	33	
<b>Parity</b>		
P0	63	36.00
P1	66	37.80
P2	23	13.10
P3	23	13.10
Not stated	69	
<b>Smoking status</b>		
Never smoker	164	81.20
Previous smoker	32	15.80
Current smoker	6	3.00
Not stated	42	
<b>Diagnosis</b>		
CD	110	45.10
UC	124	50.80
IBD-U	10	4.10
<b>Phenotype UC</b>		
UC E1	41	33.30
UC E2	48	39.00
UC E3	34	27.70
Not stated	1	
<b>Phenotype CD</b>		
A1	17	16.50
A2	85	82.50
A3	1	1.00
Not stated	7	
L1	35	33.70
L2	25	24.00
L3	44	42.30
L4	1	1.00
Not stated	6	
B1	71	71.00
B2	9	9.00
B3	20	20.00
Not stated	10	
<b>Perianal disease</b>		
Current	9	8.20
Previous	19	17.30
Previous resection surgery (all IBD patients)	54	22.10

Where numbers do not add up to 244 some data were not supplied. CD, Crohn's disease; IBD, inflammatory bowel disease; IBD-U, IBD-unclassified; UC, ulcerative colitis.

139 (59.9%) were in remission, 45 (19.4%) had mild, 41 (17.7%) moderate and 7 (3.0%) severe disease activity. Medical treatment given during pregnancy included mesalazine in 96 cases (39.7%), thiopurines (not withdrawn) in 52 cases (21.5%) and biologics in 75 cases (30.7%). Biologic treatment was stopped in 22 (29.3%) cases at a median gestational age of 28 weeks. Steroids were given in 22 cases (9.0%).

### Encounters

In total, 460 patient encounters occurred in the study cohort. Of these, 68.2% occurred as telephone encounters, while only 3% of encounters would have been conducted this way in prepandemic practice (table 2;  $p < 0.0001$ ). The number of IBD advice-line encounters was not different from prepandemic practice. Tests to assess IBD were requested in 107 encounters (23.3%) including 61 calprotectin, 11 bloods, 17 calprotectin and bloods, 8 imaging studies (5 ultrasound scans of the small bowel, 1 MRI small bowel, 2 MRI pelvis) and 4 endoscopies (1 gastroscopy, 3 sigmoidoscopies). Clinicians were asked at each encounter whether they would have provided different care outside the pandemic. In 433 encounters (94.1%), no differences in practice were reported. Divergent care occurred infrequently and included (multiple reasons per encounter possible): 12 cases tests not ordered (remote consult—blood tests not possible/calprotectin not currently offered), 4 cases where beclomethasone instead of prednisolone was used, 1 case of azathioprine not being started, 1 case of endoscopy not being available, 2 cases of patients stopping biologics prematurely against medical advice, 5 cases that would have been followed up more frequently and 3 cases that would have been examined physically if it was not for a remote consultation.

### Pregnancy outcomes

Miscarriages occurred in nine cases (3.7% of total cohort) between 5 and 13 weeks of gestation and two medical terminations of pregnancy were performed (one case of triploidy, one accidental exposure to tofacitinib in an unplanned pregnancy). At time of data cut-off for the study 123 pregnancies were ongoing. One hundred and ten women delivered 111 alive babies (one twin pregnancy) and no stillbirth occurred. Birth occurred at a mean gestational age of 38.2 weeks (median 39 weeks) with 12 (11.0%) births before 37 weeks of gestation. Birth by vaginal delivery was achieved in 62 women (56.4%; 47 normal vaginal deliveries, 15 assisted vaginal deliveries). There were no differences in the rates of vaginal delivery between CD and UC/IBD-U (53% vs 59%;  $p = 0.44$ ). Of 48 caesarean sections (43.6%), 33 were planned elective sections, while 15 were emergency caesarean sections. Of the 33 elective sections, 12 (36.4%) were undertaken for an IBD indication. The sex of the infant was known in 96 cases (50 female, 46 males) and mean birth weight was 3324 g (available for 83 infants). A low birth weight below 2500 g occurred in five cases (6.0%) only. We recorded

**Table 2** Patient encounters during the pandemic and normally planned type of patient encounter prepandemic

	Encounters	%	Normally planned encounters	%
Face to face IBD clinic	24	5.2	140	30.4
Telephone IBD clinic	148	32.2	11	2.4
Combined antenatal clinic face to face	71	15.4	174	37.8
Combined antenatal clinic telephone	102	22.2	3	0.6
IBD advice line encounter	105	22.8	101	21.9
Other encounter (infusion unit, day ward)	8	1.7	0	0
Not documented	2	0.4	31	6.7

$\chi^2$  equals 5144.742. The two-tailed P value is less than 0.0001. Normally planned encounters reflect the type of encounter that would have occurred outside the COVID-19 pandemic.

IBD, inflammatory bowel disease.

four congenital defects (one tongue tie, one cleft lip and palate, one 'boggy' head, one hypospadias/bilateral talipes). Breast feeding was recorded for 34 of 88 (38.6%) documented cases and patients exposed to biologics were not less likely to breastfeed ( $p=1$ ). Admissions to special care baby units (intermediate intensity care but not requiring neonatal intensive care) were required in 30 of 102 documented (29.4%) cases. Complications occurred in 27 cases (24.5%) and included 21 maternal labour-related problems (2 lacerations, 9 second-degree tears, 3 third degree tears, 1 post-partum haemorrhage, 1 gestational diabetes, 1 vaginal wall prolapse, 1 wound infection, 1 failed instrumental delivery). Three maternal IBD-related problems were recorded (one intestinal obstruction, one small bowel perforation, one postdelivery readmission with pain and normal cross sectional imaging). Four fetal problems included growth retardation, two cases of fetal distress and a case of meconium aspiration syndrome.

### COVID-19 infections

No documented COVID-19 infections (PCR positive) were recorded but one woman reported typical symptoms of COVID-19 including dyspnoea, dry cough and anosmia. As she did not require hospital admission, COVID-19 testing was not available to her at the time. The patient recovered without sequelae for herself or the infant.

### DISCUSSION

The COVID-19 pandemic poses a threat for patients at a higher risk of adverse outcomes,<sup>1</sup> but during the early phase of the pandemic, it was difficult to ascertain which patients fell into the high risk category. Patients with active IBD, relevant comorbidities and those on immunosuppressive therapy are considered higher risk.<sup>18</sup> It remains unclear whether pregnancy posed an additional risk factor.<sup>5</sup> In addition to the risk to the expectant mother inadequate control of inflammation from IBD is associated with adverse fetal outcomes.<sup>10</sup> Any changes to IBD antenatal care therefore posed a potential additional risk by patients potentially being lost to follow-up, avoiding

necessary medication, inability to undergo some IBD investigations and less frequent follow-up. In light of this, it is reassuring that we found a very low COVID-19 infection rate and a low rate of adverse pregnancy outcomes in a large multi-centre cohort of pregnant women with IBD in the UK.

We observed significant changes in the way that IBD antenatal care was delivered as the majority of appointments were held by telephone rather than face to face. Similar changes have occurred in general IBD clinics.<sup>17</sup> Telephone appointments are effective in a pandemic but clinician and patient may not wish to continue with this approach after the pandemic if telephone antenatal IBD care were to remain the main method of consultation. The addition of an option to conduct remote consultations after the pandemic should however be considered for those appointments where a scan or examination are not required. The medical care delivered was only altered in 6% of appointments. The IBD and obstetric services have managed to continue the delivery of safe and effective care during the pandemic. We observed only one suspected case of COVID-19, which may be attributed to remote care reducing exposure risk where appropriate, patients engaging strictly with social distancing measures and clinicians aiming to reduce patients COVID-19 risks (avoidance of systemic corticosteroids for example). In our study, it appears that pregnant women with IBD were not at excessive risk of contracting COVID-19. This may reflect patients' behaviour who may have opted to avoid social contacts. However, our sample size is insufficient to provide definite evidence on the risk of COVID-19 infection in pregnant women with IBD.

The outcomes of the 110 deliveries are reassuring, with a low rate of babies small for gestational age or delivered prematurely. We observed a caesarean section rate of 46%, which was predominantly due to elective interventions. This is somewhat in excess of the literature reporting outcomes outside the pandemic as we would have expected a 1.5 times increase over the rates seen usually in the UK general population (between 20% and 30% depending on centre).<sup>19</sup> Only about a third of these were for IBD indications and it is possible that patient

wishes and obstetric thresholds for caesarean sections could have changed during the pandemic. We also observed a lower than expected breast feeding rate of just 39%. The reason for this remains obscure but women with IBD may have wanted to reduce any potential transmission of immunosuppressive therapies to their infant during the pandemic. Interestingly, the discontinuation of biologics during pregnancy was low at 29%. In the UK, IBD services usually observe the European Crohn's and Colitis guidelines and base decisions on stopping or continuing biologics on individual risk assessments in contrast to the approach with uninterrupted biological therapy through pregnancy in American guidelines.<sup>10 20 21</sup>

Clinicians in the UK will mostly stop biologics prior to the third trimester unless the patient has active IBD or a history of difficult to control IBD. As such we assume that a shift towards more continuation of biologics occurred during the pandemic; alternatively, this could be a general change to a less conservative approach among UK gastroenterologists running specialist antenatal IBD clinics.

The strength of our study lies in a large multicentre cohort representing experiences from a diverse set of UK hospitals. This has allowed us to report on a large number of pregnancy outcomes in a relatively short period of time. There are, however, a number of limitations to our work. The study was performed in 12 UK centres with an interest in IBD antenatal care and outside these centres and indeed outside the UK, approaches to care may be different. We have previously shown that there are significant variations in UK IBD antenatal care and it is likely that the care in these 12 research active centres may differ from other non-specialist settings. The nature of predominantly retrospective data collection has led to some missing data, which may introduce bias. We have also chosen to report the findings now to inform clinicians and patients rather than to wait for all women to complete their pregnancy.

In conclusion, we have shown that despite changes to the delivery of IBD antenatal services, safe care was delivered with low COVID-19 infection rates and low rates of adverse pregnancy outcomes.

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