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The effects of pre- and post-pregnancy IBD diagnosis on birth outcomes

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The effects of pre- and post-pregnancy IBD diagnosis on birth outcomes

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3 SUMMARY
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5 Background:

6 Inflammatory bowel diseases (IBD) are frequent in women at their optimum age for reproduction.
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8 Possible effects on pregnancy are, therefore, of interest.
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10 Aim:

11 To assess pregnancy outcomes in 212 women: 135 of whom were diagnosed with IBD before
12 pregnancy and 77 after pregnancy.
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15 Methods:

16 A clinical birth database was examined retrospectively. Odds ratios (ORs) for the main outcomes
17 were calculated with 95% confidence intervals (CI); these were adjusted for confounding factors.
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20 Results:

21 Overall, pregnancy outcomes were good. No increased risk of preterm births or need for neonatal
22 intensive care was observed. However, women with IBD had more growth retarded newborns, at an
23 adjusted OR of 2.12 (1.29-3.50) and the mode of delivery was more frequently Caesarean section,
24 with an OR of 2.74 (1.81-4.13). In the women who were diagnosed with IBD after the pregnancy,
25 we found no difference in the obstetric outcome as compared to the general obstetric population.
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31 Conclusions:

32 Most women with IBD have a normal pregnancy outcome and, overall, IBD during pregnancy
33 poses low to moderate risks, the main concern being increased risk of impaired foetal growth.
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35 Normal maternal weight gain during pregnancy, possibly indicating a more stable disease, appeared
36 to protect against adverse outcomes.
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Introduction

Inflammatory bowel disease (IBD) affects patients at the age when they are most fertile, the highest incidence is in individuals in their 20s and 30s. The mean age at diagnosis is between 31.4 and 31.8 years (1,2).

Because of the nature of IBD and its early age of onset, there has been concern about its effects on pregnancy outcomes. Some studies have shown that IBD is associated with a possible 3-fold increase in the risk of preterm delivery (3,4) and 2-9-fold risk in the risk of low birth weight (LBW), i.e. under 2500g (3,5,6). Accordingly, a 4-6 fold increase in the risk of foetal growth restriction (small for gestational age (SGA)) has been reported (7,8). Furthermore, it has been reported that the risk of a Caesarean section (CS) being required is 1.5-9 times greater in women suffering from IBD (1,3,7). Reports have even suggested a 7-fold increase in the risk of stillbirth (9) and 2-4-fold risk of congenital abnormalities for patients with UC (3,7).

Only a few studies have been published that examine pregnancies before IBD-diagnosis in women who eventually develop either UC or CD. These studies suggest that pregnancy outcomes are affected prior to diagnosis. Specifically, the risk of preterm delivery has been reported as being up to ten times greater (10,11) and the risk of low birth weight up to eight times greater (12).

The objective of this study was to determine the outcomes of pregnancy in women with IBD and to compare the pregnancies of the same women in the time period prior to IBD diagnosis.

Methods

A retrospective analysis was conducted of an existing database containing information about patients with bowel diseases, focussing on women of reproductive age. The database comprises information on all patients (n=1303) diagnosed or treated at Kuopio University hospital for IBD. Data pertaining to family history, the onset of the disease, type and anatomical location of the disease, medication, surgical treatment and complications were collected and updated as part of the hospital's clinical work. The diagnosis of IBD was routinely confirmed by colonoscopy and biopsies. Data pertaining to all the pregnancies (n=212) of women on the IBD-register were collected from the Kuopio University Hospital birth register, which contains information on all women who gave birth at Kuopio University Hospital between 1989 and 2006. Women with a

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3 diagnosis of UC or CD before the year of delivery were included in the UC and CD groups,
4 respectively. If the diagnosis of IBD was made during the same year as the delivery or after the
5 delivery, the women were included in the pre-UC and pre-CD groups. These groups were compared
6 to the entire obstetric population, which acted as the reference group, and to each other. For further
7 analysis, the UC and CD subgroups were pooled into an IBD-group and the pre-UC and pre-CD
8 subgroups into a pre-IBD group. Numbers of women in each study group are presented in Figure 1.
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16 Exclusion criteria were: (1) multiple pregnancies, i.e. twins, triplets and higher order pregnancies
17 and (2) major foetal structural anomalies, because such pregnancies carry an unusually high risk of
18 adverse outcome, and the effect of maternal IBD on these pregnancies would be difficult to
19 distinguish. A total of 38,497 pregnancies were included in the analyses.
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25 Information on maternal characteristics was based on data from self-administered questionnaires at
26 approximately 20 weeks of pregnancy. When any data were missing, the gaps were filled in by
27 interviews conducted by a nurse on the delivery ward. The questionnaire consisted of 75
28 background items. Information on maternal medication, pregnancy complications, pregnancy
29 outcome and the neonatal period was collected in real time, as part of clinical work, by the nurses
30 and midwives who undertook delivery and neonatal care. The Institutional Review Board accepted
31 the study and childbearing women gave informed consent at the time of data collection. The ethical
32 committee has accepted the database and given permission for its use for research purposes. The
33 data were processed in such a way that individuals could not be identified.
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41 Kuopio University Hospital is a tertiary level obstetric referral centre, but it is also the only
42 obstetric hospital in our district. During data collection, antenatal care was readily and easily
43 accessible to all women. Home deliveries were exceptional, and therefore not included.
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49 Definitions of the background and outcome variables are listed in supplementary on-line material,
50 Table 1. Estimation of gestational age was based on menstrual history and ascertained by measuring
51 foetal crown–rump length by ultrasonography, in approximately 95% of cases, at 10 to 12 weeks of
52 pregnancy. If a subject had two adverse pregnancy outcomes, for example LBW and preterm
53 delivery, each was treated as an independent outcome and the subject was included in both
54 categories. The pregnancy complications chorio-amnionitis, placental abruption and placenta
55 praevia were recorded when these obstetric diagnoses were made during the hospital stay.
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Abnormal fetal heart rate (cardiotocogram, CTG) was recorded in the database by obstetricians.
Meconium staining of the amniotic fluid during delivery was noted in the delivery reports and

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3 entered into the database by midwives. Apgar scores were assessed mainly by midwives in
4 uncomplicated deliveries and by paediatricians, when consulted.
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9 Statistical differences between the subjects and the reference group were evaluated using Chi-
10 square tests (dichotomous variables), and Fisher's exact test was applied when the minimal
11 estimated expected value was less than five. A value of $p < 0.05$ was considered statistically
12 significant. Continuous variables were analysed using two-tailed, pooled t tests and standard
13 deviations (\pm SD) were calculated. Logistic regression analysis, controlling for all possible clinically
14 significant confounding factors, was performed using SAS for Windows (SAS statistical package
15 release 8). In the first analysis, unadjusted ORs were calculated (OR). The logistic regression
16 models included the variables: age if under 18 years, age if over 35 years, maternal BMI, smoking
17 during pregnancy, primiparity, multiparity and scarred uterus. In the second and third models, the
18 possible causal factors anaemia and poor maternal weight gain were added separately into the
19 analysis. In the fourth model, anaemia and poor maternal weight gain were simultaneously included
20 in the analysis. Confidence intervals were evaluated at 95%.
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32 Results

33 At the University Hospital of Kuopio the frequency of IBD was 0.35 % of all pregnancies
34 progressing beyond 22 weeks; this equated to one in 284 pregnancies. Women, who had a diagnosis
35 of UC or CD prior to pregnancy (IBD-group, $n=135$) were significantly older than women in the
36 reference group (29.9 ± 5.50 vs. 29.0 ± 5.5 y, $p=0.04$). Maternal weight gain during pregnancy was
37 significantly lower in the UC-group and IBD-group than in the reference group ($12.3 \pm$ SD 5.8 kg
38 vs. $13.5 \pm$ SD 5.6 kg, $p=0.05$; $12.3 \pm$ SD 6.1 kg vs. $13.5 \pm$ SD 5.6 kg, $p=0.01$, respectively), although
39 at the beginning of pregnancy, there were no significant differences in the mean maternal BMIs
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48 Birth weight of newborns in the UC-group and in the IBD-group was significantly lower than it was
49 in the reference group ($3317 \pm$ SD 658g vs. $3506 \pm$ SD 613g, $p=0.003$; $3340 \pm$ SD 631g vs. $3507 \pm$ SD
50 613g, $p=0.002$, respectively). Newborns in the CD-group were also smaller than those in the
51 reference group but the difference was not statistically significant.
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56 Reproductive risk factors, along with maternal and pregnancy characteristics, are shown in
57 supplementary on-line material, Table 2. Women in the UC- and IBD-groups had undergone more
58 induced abortions prior to the current pregnancy than women in the reference group (19.0% vs.
59 10.7%, $p=0.009$; 17.8% vs. 10.7%, $p=0.008$, respectively). Primiparous women were less frequent
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3 in the UC-group than in the reference group (28.4% vs. 41.2%, $p=0.01$). Prior uterine operations
4 were also more common in the UC-group and IBD-group than in the reference group (21.1% vs. 9.7
5 %, $p<0.001$; 17.8% vs. 9.7%, $p=0.002$, respectively). Other maternal characteristics, specifically
6 prior miscarriages, prior stillbirths, age ≥ 36 years, unmarried status, overweight, smoking, drinking
7 alcohol and hypertension did not differ significantly between the study and reference groups.
8 Modes of delivery and pregnancy outcomes are shown in supplementary on-line material, Table 3.
9 Anaemia during the third trimester was more common in women in the UC- and IBD-groups than in
10 the reference group (6.3% vs. 1.7%, $p<0.001$; 5.9% vs. 1.7%, $p<0.01$, respectively). Pregnancy
11 morbidity of the study groups and the reference group were similar as regards gestational diabetes,
12 pre-eclampsia, placenta praevia, chorioamnionitis and placental abruption.
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23 Significantly higher incidence of adverse pregnancy outcomes were recorded in women with
24 diagnosed UC or CD compared with the reference group (supplementary on-line material, Table 3).
25 Caesarean section was a more likely mode of delivery in the UC- and IBD-groups than in the
26 reference group (33.7% vs. 17.0%, $p=0.01$; 31.9% vs. 17.0%, $p<0.001$, respectively). SGA was also
27 more common in the UC-and IBD-groups than in the reference group (16.8 % vs. 9.4%, $p=0.014$;
28 15.6% vs. 9.4%, $p=0.015$, respectively). The need for neonatal intensive care was higher in the CD-
29 group than in the reference group (20.0% vs. 8.7%, $p=0.02$). There were no statistically significant
30 differences in maternal or pregnancy characteristics or in pregnancy outcomes between the group of
31 women diagnosed with IBD after pregnancy and the reference group. No differences between the
32 study groups and the reference group were observed in the incidences of vacuum assisted delivery,
33 abnormal fetal cariotocogram during delivery, umbilical vein pH at birth, Apgar scores at the age of
34 five minutes, preterm births or low birth weight under 2500g. Table 4 in supplementary on-line
35 material lists the maternal and foetal anthropometric variables, weight gain and hemoglobin in the
36 study groups compared to the reference group.
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48 The results of the logistic regression analysis models comparing main pregnancy outcomes in the
49 healthy reference mothers and the study groups are presented in table 5. When adjusted for
50 confounding factors and anemia and low weight gain, women who had IBD were more likely to
51 require delivery by Caesarean section (adjusted OR 2.75; 95% CI 1.82-4.16) and low birth weight
52 for the gestational age (adjusted OR 2.08; 95% CI 1.26-3.44).
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58 Of the 135 mothers who had IBD during pregnancy, 70 (51.9%) **had drug treatment either for active**
59 **disease or as a maintenance medication:** mesalazine in 60 (44.4%) patients, systemic prednisolon in
60 19 (14%), sulfasalazine in 10 (7.4%), azatioprin in 2 (1.5%) and cyclosporine in 1 (0.7%) patient.

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3 In subgroup analyses, there was no difference in the incidence of anemia (7.1% vs 4.6%,
4 respectively, $p=0.53$) in medicated women compared with women who had no medication; nor in
5 the incidence of low birth weight under 2500 g (8.6% vs. 6.2%, respectively, $p=0.59$); nor in the
6 incidence of birth weight small for gestational age (14.3% vs. 16.9%, respectively, $p=0.67$).
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10 11 Discussion

12 IBD was a factor in 0.35% of all deliveries at the Kuopio University Hospital. Thus, the frequency
13 of IBD is comparable to its prevalence in Europe (13). However, in a clinical setting the criteria
14 used for diagnosis may vary and some of the cases may go undiagnosed if clinical signs are not
15 present or are mild. Although rare, the conditions involved are of concern to affected women and
16 their doctors.
17

18 The main finding of the present study was that the overall risk of an adverse obstetric outcome was
19 moderately low, although a doubled risk of foetal growth limitation (SGA) was recorded in affected
20 women. Second, our results showed that the effect on foetal growth was clearly associated with the
21 onset of the disease, since there was no risk of impaired foetal growth in women who were
22 diagnosed with IBD after pregnancy. In other words, genetic factors and foetal growth potential
23 have no major role to play herein. Third, pregnancies proceeded normally with respect to most
24 factors considered, although the mean haemoglobin concentration and maternal weight gain were
25 lower in affected women than in the reference group and this difference was statistically significant.
26 Although these differences were of limited clinical significance, it is noteworthy that the risk of
27 third trimester maternal anaemia was more than three times higher in women with IBD. Fourth,
28 Caesarean deliveries were more common for the affected group than the reference group. Finally,
29 the need for neonatal intensive care was higher among infants born to mothers affected by CD.
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45 A number of studies have suggested that women with IBD during pregnancy are exposed to a
46 substantial risk of adverse outcomes (3,6). A recent meta-analysis by Cornish et al (3) concluded
47 that women with IBD included in studies published since 2000 were more likely to experience
48 premature birth (OR: 1.99 95 % CI: 1.22-3.26)(4,5,7,14,15), congenital abnormalities in the infant
49 (OR: 2.39; 95 % CI: 1.28-4.48)(4,7,16) and Caesarean sections (OR: 1.54; 95 % CI: 1.24-1.91))
50 (4,5,7,14,15), but not SGA (OR:1.79; 95 % CI: 0.66-4.82)(4,5,7,8,17,18). However, two studies that
51 were also included in the meta-analysis, did report an increased risk of SGA (7,8) Premature births
52 occurred up to 30% more often in the current study, but the difference was not statistically
53 significant; in contrast we found that the risk of SGA was significantly increased even after
54 adjusting for confounding factors.
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5 The outcome differences between our results and those in previous studies may be because only
6 women with pregnancies going beyond 22 weeks were considered in the present study. Pregnancies
7 ending with miscarriages in the first or early second trimester were not included, and therefore it is
8 possible that women suffering from severe bowel disease were excluded. On the other hand, the
9 number of previous miscarriages was statistically similar in affected and unaffected women.
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12 Another possible explanation is that the disease activity at the time of conception or in the course of
13 pregnancy was not comparable in the different studies, thus affecting the premature birth rates.
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16 However, the significantly increased risk of SGA, both unadjusted and adjusted, remains to be
17 explained. Interestingly, the correction for low maternal weight gain and anaemia appeared to
18 somewhat reduce, but not eliminate, the SGA risk. Medication during pregnancy seemed not to be
19 the explanation for increased risk of SGA, since women with no medication had similarly increased
20 risk. **Unfortunately, we could not analyze the role of active disease in this retrospective study.**
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23 **The results of the current study according women diagnosed with IBD after the pregnancy**
24 **are based on a limited population and should be confirmed in future studies with larger**
25 **populations, reaching higher statistical power.**
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29 The clinical importance of an increased rate of SGA in affected births is considerable, since an
30 underweight full term infant has a four times higher risk of severe morbidity compared to an infant
31 of normal weight (19). Specifically, these infants have increased risks of asphyxia, meconium
32 aspiration and hypoglycaemia (20). In addition, low birth weight of a full term infant has been
33 associated with increased incidence of the risk factors associated with coronary heart disease, such
34 as insulin resistance, glucose intolerance, type II diabetes mellitus and elevated blood pressure in
35 adulthood (21-23).
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3 IBD is usually preceded by a preclinical phase, when the patients are not yet diagnosed and have
4 not yet sought medical help. The preclinical phase of the disease may, however, be associated with
5 health issues. Thus, in the present study we investigated whether preclinical IBD has any impact on
6 pregnancy outcome. We did not observe any differences in the pregnancy outcomes of women who
7 were pregnant before the diagnosis of CD or UC and the reference group. A few other studies have,
8 similarly, found no association between pre-diagnosis IBD and pregnancy outcome (9,24). In the
9 present study we had no opportunity to assess pregnancy outcome of the same women before and
10 after IBD diagnosis, the setting possibly offering new perspectives to the problem.

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12 On the other hand, our results contradict a few previous studies that have reported a higher preterm
13 birth rate and lower mean birth weight of infants born to women with preclinical CD compared with
14 a reference group (10-12). In addition, Caesarean section has been reported to be more common in
15 women who eventually developed CD or UC than in an equivalent reference group (11).

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17 Furthermore, there is one report of a higher rate of preterm deliveries in pre-diagnosis CD and UC
18 than in a reference population (10).

19
20 We conclude that, in most cases, the pregnancy outcome of the IBD patients considered was good,
21 with no increase in the rate of preterm births or neonatal intensive care, the associated problems of
22 fetal growth restriction and more caesarean sections being clinically less severe. This may be partly
23 due to the antenatal care that was readily and easily accessible to all women. Thus, the commonly-
24 held fears about childbirth recently reported among IBD-patients (25) are not justifiable on the basis
25 of the results of the current study. However, pregnancies in women with IBD should be considered
26 to be associated with a low to moderate risk, depending on the activity of the disease. Therefore,
27 monitoring at specialized maternity clinics appears to be advisable, aiming at early recognition and
28 adequate treatment of growth restricted foetuses.

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3 Statement of Interests
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6 All authors declare that they have no conflicting interests.
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13 Financial support
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16 There is no external financial support for this study.
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For Peer Review

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Figure1. Number of patients in the study groups

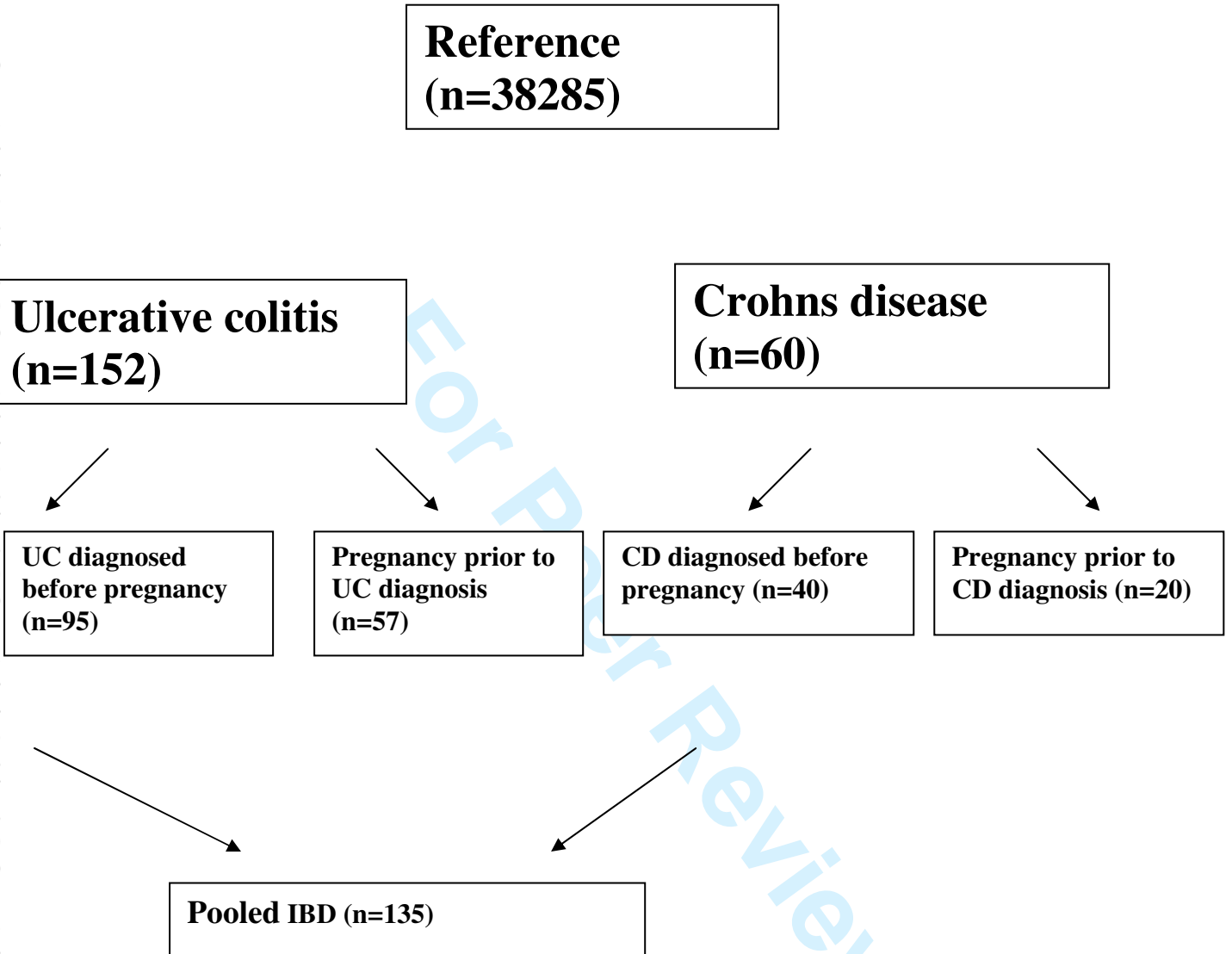


Table 5: Mode of delivery and pregnancy outcome in the study groups compared to the reference group

Study group	Reference (n=38,285)	%	UC (n=95)	%	Pre-UC (n=57)	%	CD (n=40)	%	Pre-CD (n=20)	%	IBD (n=135)	%	Adjusted OR, IBD compared with reference ¹
Caesarean section	6508	17.0	32	33.7**	9	15.8	11	27.5	2	10	43	31.9**	2.75 (1.82-4.16)
Premature birth <37 pregnancy weeks	2352	6.1	9	9.5	3	5.3	3	7.5	0	0	12	8.9	1.23 (0.60-2.54)
Low birth weight < 2500g	1796	4.7	7	7.4	3	5.3	3	7.5	0	0	10	7.4	1.83 (0.88-3.80)
Small for gestational age	3609	9.4	16	16.8**	7	12.3	5	12.5	2	10	21	15.6**	2.08 (1.26-3.44)
Neonatal intensive care	3333	8.7	9	9.5	1	1.8	8	20**	3	15	17	12.6	1.64 (0.96-2.79)

*p<0.05, **p<0.01. ***p<0.001 compared to the reference group of general obstetric population

Abbreviations: UC ulcerative colitis, pre-UC ulcerative colitis diagnosed after pregnancy, CD crohns disease, pre-CD crohns disease diagnosed after pregnancy, IBD inflammatory bowel disease, pooled UC and CD

¹ Adjusted for: young age under 18 years, old age over 35 years, body mass index (categorical 20-25 vs. ≤19, 26-29 and ≥ 30), parity (primiparous or parous), smoking during pregnancy (yes/ no), prior uterine scarring and anaemia and low weight gain ≤9kg (Model 4)

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For Peer Review

Table 1. Definitions of background variables and outcomes

Unmarried	Civil status other than marriage: cohabiting, single, widowed or divorced
Parity	Primiparous or parous, number of prior births
Prior induced abortion	Induced abortion of a viable foetus, as distinct from miscarriage
Prior stillbirth	Intrauterine death of a foetus over 22 weeks gestational age or over 500 g
Overweight	Pre-pregnancy body mass index (BMI) over 25 kg/ m ²
Smoking	Self reported smoking yes/ no
Alcohol use	Self reported alcohol use yes/ no
Chronic illness	Conditions requiring regular medication that have a possible effect on pregnancy: thyroid disease, arthritis, epilepsy, cardio-vascular and kidney diseases
Low haemoglobin	Hb under 100 g/l
Pre-eclampsia	Repeated blood pressure measurement exceeding 140/90 mmHg with proteinuria exceeding 0.5 g/day
Preterm birth	Delivery before 37 weeks gestation
Small for gestational age	Age- and sex-adjusted birth weight below the tenth percentile according to the normal tables for our population (27)
Low birth weight	Birth weight less than 2500 g
Mode of delivery	Spontaneous, instrumental or Caesarean section
Apgar scores	Low when the scores were less than 7
Foetal acidosis	pH 7.15 at birth in the umbilical vein
Neonatal intensive care	Infants requiring more than 24 hours surveillance
Foetal death	Intrauterine death of a foetus over 22 weeks gestational age or over 500 g
Neonatal death	Death during the first seven days after birth

Table 2: Occurrence and trend of maternal pre-pregnancy characteristics and morbidity in study groups compared to the reference group

	Reference	%	UC	%	Pre-UC	%	CD	%	Pre-CD	%	IBD	%
	(n=38285)		(n=95)		(n=57)		(n=40)		(n=20)		(n=135)	
Primiparous	15766	41.2	27	28.4**	29	50.9	18	45.0	6	30.0	45	33.3
Prior miscarriage	6791	17.7	20	21.1	13	22.8	2	5.0	3	15.0	22	16.3
Prior stillborn	629	1.6	0	0.0	1	1.8	0	0.0	0	0.0	0	0.0
Prior induced abortion	4079	10.7	18	19.0**	4	7.0	6	15.0	3	15.0	24	17.8
Surgically scarred uterus	3720	9.7	20	21.1**	4	7.0	4	10.0	1	5.0	24	17.8**
Age \geq 36 years	4812	12.6	12	12.6	4	7.0	6	15.0	3	15.0	18	13.3
Not married	13941	36.4	37	39.0	18	31.6	16	40.0	5	25.0	53	39.3
BMI \geq 26 before pregnancy	8193	21.4	27	28.4	10	17.5	9	22.5	4	20.0	36	26.7
Smoked before pregnancy	9551	25.0	21	22.1	8	14.0	15	37.5	5	25.0	36	26.7
Used alcohol before pregn.	14520	37.9	40	42.1	22	38.6	13	32.5	9	45.0	53	39.3
Chronic illness	3305	8.6	8	8.4	6	10.5	7	17.5	0	0.0	15	11.1
Hypertonia arterialis	1159	3.0	5	5.3	3	5.3	2	5.0	0	0.0	7	5.2
Third trimester anaemia	662	1.7	6	6.3**	1	1.8	2	5.0	0	0.0	8	5.9**
Gestational diabetes	2401	6.3	7	7.4	1	1.8	2	5.0	0	0.0	9	6.7
Pre-eclampsia	1134	3.0	5	5.3	2	3.5	1	2.5	0	0.0	6	4.4
Gestational hepatitis	272	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Placenta praevia	151	0.4	2	2.1	0	0.0	0	0.0	0	0.0	2	1.5
Chorioamnionitis	418	1.1	0	1.1	2	3.5	0	1.1	0	1.1	0	1.1
Placental abruption	253	0.7	1	1.1	1	1.8	0	0.0	0	0.0	1	0.7

*p<0.05, **p<0.01. ***p<0.001 compared to the reference group; UC =ulcerative colitis, CD= Crohns disease, Pre=diagnosed after index pregnancy

Table 3: Mode of delivery and pregnancy outcome in the study groups compared to the reference group

Study group	Reference (n=38285)	%	UC (n=95)	%	Pre-UC (n=57)	%	CD (n=40)	%	Pre-CD (n=20)	%	IBD (n=135)	%
Caesarean section	6508	17.0	32	33.7**	9	15.8	11	27.5	2	10	43	31.9**
Vacuum delivery	2316	6.1	3	3.2	2	3.5	4	10	0	0	7	5.2
Abnormal CTG	5053	13.2	14	14.7	6	10.5	6	15	2	10	20	14.8
Umbilical vein pH under 7.15 at birth	462	1.2	2	2.1	0	0	0	0	0	0	2	1.5
5 minute Apgar score under 7	689	1.8	0	0	2	3.5	0	0	0	0	0	0
Premature birth	2352	6.1	9	9.5	3	5.3	3	7.5	0	0	12	8.9
Low birth weight < 2500g	1796	4.7	7	7.4	3	5.3	3	7.5	0	0	10	7.4
Small for gestational age	3609	9.4	16	16.8**	7	12.3	5	12.5	2	10	21	15.6**
Neonatal intensive care	3333	8.7	9	9.5	1	1.8	8	20**	3	15	17	12.6

CTG= cardiotocogram

*p<0.05, **p<0.01. ***p<0.001 compared to the reference group; UC =ulcerative colitis, CD= Crohns disease, Pre=diagnosed after index pregnancy

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Study group	Reference (n=38285)	UC (n=95)	Pre-UC (n=57)	CD (n=40)	Pre-CD (n=20)	IBD (n=135)
Mother						
Age of mother	29.0±5.5	30.0±4.9	27.4±4.9**	29.8±5.4	28.0±6.4	29.9±5.0**
Weight gain	13.5±5.6	12.3±5.8**	12.9±4.5	12.1±6.8	18.3±13.8	12.3±6.1**
BMI before pregnancy	23.2±4.4	24.0±4.3	22.6±3.5	23.5±4.1	22.4±3.2	23.8±4.3
BMI at birth	28.1±4.4	28.8±4.3	27.6±4.1	27.8±4.1	29.5±5.2	28.5±4.2
Hb I trimester	128.7±14.3	125.6±11.8**	128.9±11.3	123.4±12.7	127.4±7.4	124.9±12.0**
Hb II trimester	118.5±9.2	115.3±9.9**	118.4±9.6	114.1±15.2	116.1±7.5	115.0±11.6**
Hb III trimester	119.7±9.7	116.4±11.2**	120.2±10.1	114.6±13.4	118.9±8.1	115.9±11.8**
Newborn						
Birth weight (g)	3506.6±613.2	3317.1±658.2**	3522.8±614.1	3397.3±566.8	3507.5±460.6	3340.9±631.5**
Head circumference (cm)	35.0±2.9	34.6±2.0	35.0±1.4	35.3±2.9	34.8±1.3	34.8±2.3
Abdominal circumference (cm)	33.9±3.4	33.5±2.0**	33.6±1.8	33.4±2.2	33.8±1.7	33.4±2.1**
Height (cm)	50.0±4.7	49.6±2.7	50.7±1.9**	49.9±2.6	50±1.9	49.7±2.7
Weight of placenta (% of birth weight)	18.4±5.6	18.5±3.5	16.6±3.2**	18.4±4.4	17.6±2.4	18.5±3.8
Pregnancy duration (weeks)	39.3±2.2	38.8±2.6	39.5±1.8	39.2±1.9	39.6±1.3	38.9±2.4
*p<0.05, **p<0.01. ***p<0.001 compared to the reference group UC =ulcerative colitis, CD= Crohns disease, Pre=diagnosed after index pregnancy						