Published in final edited form as:

Dig Dis Sci. 2016 August ; 61(8): 2381–2388. doi:10.1007/s10620-016-4076-7.

Factors Associated with the Success of In Vitro Fertilization in Women with Inflammatory Bowel Disease

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Electronic supplementary material The online version of this article (doi:10.1007/s10620-016-4076-7) contains supplementary material, which is available to authorized users.

Author contributions: Sveta Shah Oza, MD, contributed to the study concept and design, acquisition of data, analysis and interpretation of data, and drafting of the manuscript; Vikas Pabby, MD, contributed to study concept and design, acquisition of data, and analysis and interpretation of data; Laura E. Dodge, MPH, and Michele R. Hacker, ScD, analyzed and interpreted the data and drafted the manuscript; Janis H. Fox, MD, designed the study and analyzed and interpreted the data; Vasiliki A. Moragianni, MD, MS, was involved in study design, acquisition of data, and analysis and interpretation of data; Katharine Correia, MPH, and Stacey A. Missmer, ScD, contributed to study design and analysis and interpretation of data; Yetunde Ibrahim, MD, was involved in acquisition of data; Alan Penzias, MD, and Robert Burakoff, MD, contributed to study concept and design and analysis and interpretation of data; Sonia Friedman, MD, and Adam S. Cheifetz, MD, was involved in study concept and design, acquisition of data, analysis and interpretation of data, and drafting of the manuscript.

Compliance with ethical standards: Conflict of interest: Adam S. Cheifetz: Consulting/research: Janssen, Abbvie, Takeda, Pfizer, UCB, Prometheus; Alan Penzias: Advisory Board (with compensation): OvaScience; Nora Therapeutics; Consultant: ReproSource, Inc; Speakers Bureau: Ferring Pharmaceuticals; Michele R. Hacker: Support from Harvard Catalyst | The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award UL1 TR001102) and financial contributions from Harvard University and its affiliated academic healthcare centers; Sveta Shah Oza, Vikas Pabby, Laura E. Dodge, Vasiliki A. Moragianni, Janis H. Fox, Katherine Correia, Stacey A. Missmer, Yetunde Ibrahim, Robert Burakoff, and Sonia Friedman have no disclosures or conflicts of interests.

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Abstract

Background—It is unknown whether certain factors are associated with the success of in vitro fertilization (IVF) in women with inflammatory bowel disease (IBD).

Aim—This study assessed whether certain characteristics are associated with greater success of live birth following IVF.

Methods—In a cohort study of 8684 women with IBD seen at two tertiary care centers, we identified 121 women with IBD who underwent IVF. We assessed the effect of numerous factors on likelihood of achieving live birth after IVF.

Results—Seventy-one patients with ulcerative colitis (UC) and 49 patients with Crohn's disease (CD) were analyzed. Patients with UC who achieved a live birth were younger ($p = 0.03$), had a shorter duration of disease ($p = 0.01$), and were more likely to be in remission ($p = 0.03$) versus those who did not achieve live birth. Patients with CD who achieved live birth were younger ($p < 0.001$), had lower body mass index (BMI) ($p = 0.02$), and had lower cycle day 3 follicle-stimulating hormone levels ($p = 0.02$). There was no difference in likelihood of achieving live birth among patients in remission and those with mild or unknown disease status ($p = 0.69$), though most CD patients (79.5 %) were in remission. Prior surgery was not associated with live birth in patients with UC ($p = 0.31$) or CD ($p = 0.62$).

Conclusions—As in the general infertility population, younger patients and those with lower BMI were more likely to achieve live birth. History of surgery was not associated with live birth among IBD patients. This is important information for practitioners counseling IBD patients.

Keywords

In vitro fertilization; Crohn's disease; Ulcerative colitis; Infertility; Outcomes

Introduction

Inflammatory bowel disease (IBD) often affects women during peak reproductive age, thereby calling into question its impact on fertility. Crohn's disease (CD) and ulcerative colitis (UC) may affect fertility in several ways. Patients may choose not to have children due to several concerns, including the effect of pregnancy on disease, the possibility of passing on a diagnosis of IBD to a child, or the stress of raising a child in the setting of concomitant disease burden [1, 2]. Decrease in sexual function may also impact overall fertility, as IBD is related to poor body image, dyspareunia, and decreased sexual activity [3–5].

The most significant factor influencing fertility in the IBD population is surgery, specifically total proctocolectomy with ileal pouch anal anastomosis (IPAA) in women with UC. This subgroup of patients has an increased risk of infertility compared to the general IBD population, which is thought to be related to tubal factors secondary to surgery [6–8].

In the general population, many women with infertility seek assisted reproductive techniques such as in vitro fertilization (IVF) to assist in achieving pregnancy. IVF is a procedure by which oocytes are retrieved from the ovaries and co-incubated with sperm following oocyte maturation. The resulting embryos are then transferred into the uterus. In the non-IBD population, the likelihood of IVF success is influenced by various factors, including age, body mass index (BMI), and level of cycle day three follicle-stimulating hormone (CD3 FSH), which is a marker of ovarian reserve.

We recently described the outcomes of IVF in 121 patients with IBD and found that women with CD and UC achieved similar rates of live birth after up to six cycles of IVF when compared to 470 matched women without IBD from the general infertility population [9]. A sub-analysis of this study demonstrated that 22 women with UC and IPAA achieved similar rates of live birth when compared with women with UC without IPAA and with 470 matched infertile women without IBD [10].

It is not known whether certain factors, including IBD disease characteristics, affect the success of IVF (as measured by the live birth rate). It is conceivable that medication use, extent of disease, length of diagnosis, or history of surgical treatments other than IPAA could affect the success of IVF. Furthermore, it is important to know whether disease activity affects the likelihood of live birth following IVF. Therefore, the aim of this study was to determine whether there are specific diseases or reproductive characteristics that influence the success of IVF.

Methods

This is a sub-analysis of a matched retrospective cohort study assessing success of IVF in women with IBD compared to women without IBD. The larger original study included women with IBD seen from 1998 through 2011 at two large tertiary care hospitals, Beth Israel Deaconess Medical Center (BIDMC; Boston, MA) and Brigham and Women's Hospital (BWH; Boston, MA) [9]. A total of 8684 women with IBD were identified via ICD-9 codes 555.x and 556.x. Of these, 121 IBD patients underwent fresh, non-donor IVF at Boston IVF (an affiliate of BIDMC; Waltham, MA) and Brigham and Women's Center for Infertility and Reproductive Surgery (Boston, MA) from 1998 through 2011 following their IBD diagnosis, which was confirmed by chart review. Patients were excluded from the study if the IBD diagnosis followed IVF or if a gestational carrier was used. Patients were followed up until discontinuation of treatment, completion of six IVF cycles, or live birth, whichever occurred first.

The analysis presented here assesses factors influencing live birth following IVF. Reproductive characteristics assessed include age, BMI, parity, levels of CD3 FSH and peak estradiol, infertility diagnosis, number of IVF cycles, use of assisted hatching and

intracytoplasmic sperm injection, and the number of embryos cryopreserved (a marker of success of ovarian stimulation). Disease characteristics evaluated include length of disease diagnosis, current and past medications, surgical treatment, and disease severity. Disease activity was determined retrospectively based on chart review. For UC, disease activity was assessed using the partial Mayo score, with a score of 0 or 1 considered indicative of clinical remission. In those patients who had total proctocolectomy with IPAA, this scoring system could not be applied. Instead, patients with UC who had IPAA were designated as having either “active” or “inactive” disease, where active disease status indicated symptoms at the time of IVF including increased frequency of bowel movements, pain, fecal urgency, or rectal bleeding. For CD, disease severity was assessed using the Harvey–Bradshaw Index (HBI), where a score of 4 or less indicated remission.

The institutional review boards of BIDMC and BWH approved the study.

Data are presented as the median with interquartile range (IQR) or frequency and proportion. Patients were grouped by whether they achieved a live birth by the end of six IVF cycles, and characteristics were compared using the Wilcoxon rank sum test for continuous variables and the Chi-square or Fisher's exact test for categorical variables, as appropriate. Pearson correlation coefficients were used to evaluate correlations between age and length of IBD diagnosis. All analyses were conducted using SAS 9.4 (SAS Institute, Cary, North Carolina) and Stata 12 (Stata-Corp, College Station, Texas). All tests were two-sided. p values <0.05 were considered statistically significant.

Results

One hundred twenty-one patients with IBD who underwent IVF were included in this analysis. Of these, 71 patients had a diagnosis of UC, 49 had CD, and one patient had IBD unclassified. After up to six cycles of IVF, 69.0 % of the patients with UC and 57.1 % of the patients with CD had achieved a live birth.

At the time of their first IVF cycle, the median age of women with UC was 35.1 years of age (32.6–39.0). Among these women, those with a live birth were younger than those without a live birth (34.1 vs. 37.7 years, $p = 0.03$; Table 1). Median BMI was lower among women with a live birth than among those without a live birth (22.5 vs. 24.0, $p = 0.06$), though the difference was not significant. Parity, level of CD3 FSH, and infertility diagnosis did not differ significantly between women with UC who did and did not have a live birth (all $p > 0.11$).

Similar to patients with UC, age was associated with achievement of live birth in women with CD. Women with a live birth had a younger median age at first cycle than those without a live birth (32.3 vs. 39.1 years, $p < 0.001$; Table 2), and median BMI was significantly lower among patients with a live birth compared to those without a live birth (21.8 vs. 25.0, $p = 0.02$). Median levels of CD3 FSH were also lower among women with CD who had a live birth compared to those without a live birth (6.6 vs. 9.1 mIU/ml, $p = 0.02$). Parity and infertility diagnosis were not associated with live birth in patients with CD.

Patients with UC were diagnosed a median of 8.9 years (4.6–15.0 years) prior to their first IVF cycle. Those who achieved a live birth by the end of IVF treatment had a shorter median length of diagnosis compared to those who did not achieve a live birth (6.7 vs. 14.8 years, $p = 0.01$; Table 3). Age was not significantly correlated with duration of UC diagnosis ($r = 0.18$, $p = 0.17$). Surgical treatment with total proctocolectomy with IPAA or total proctocolectomy with ileostomy was not associated with achievement of live birth ($p = 0.51$ and $p = 0.17$, respectively). Medication with 5-aminosalicylates, glucocorticoids, immunomodulators, or antibiotics in the past or at the time of IVF was not associated with achievement of live birth. Although the total number of patients on biologics was small, use of past biologic therapy prior to IVF treatment was greater among patients who did not achieve a live birth compared to those who did achieve a live birth (13.6 vs. 0 %, $p = 0.03$).

A total of 84.8 % of patients were in clinical remission at the time of IVF. Of the 49 patients with UC who did not have an IPAA, 88.3 % of those who achieved a live birth were in clinical remission, compared to 75.0 % of patients who did not achieve a live birth ($p = 0.28$). Of those patients who had a live birth, 82.4 % had a partial Mayo score of 0, compared with 50.0 % of patients who did not achieve a live birth ($p = 0.03$; Table 3). The proportion of other disease activity states did not differ between patients who did and did not achieve a live birth (all $p \geq 0.10$).

There was no difference in the achievement of live birth among patients with UC in remission with a score of 0 or 1 and those with partial Mayo scores of 2 and 3 ($p = 0.62$).

Among patients with UC who had IPAA, there was no significant difference in disease activity between those who did and did not achieve a live birth (all $p \geq 0.48$; Table 3).

Patients with CD were diagnosed a median of 10.3 years (IQR 5.6–16.1 years) prior to their first IVF cycle, and this did not differ between those who did and did not achieve a live birth ($p = 0.41$; Table 4). Age was not significantly correlated with length of CD diagnosis ($r = 0.26$, $p = 0.10$). Past medications, current medications, and past surgery did not differ between the two groups (all $p \geq 0.06$).

A total of 79.5 % of patients with CD were classified as being in remission at the time of IVF. Of the patients who achieved a live birth, 83.3 % were in remission, compared to 73.3 % of the patients who did not achieve a live birth ($p = 0.69$). Among all CD patients, 12.8 % had mild disease, and 3.3 % had an unknown HBI at the time of IVF. Excluding patients with unknown disease activity, the prevalence of remission as compared to mild disease did not differ between those who achieved a live birth (90.9 %) and those who did not achieve a live birth (78.6 %; $p = 0.36$).

For both UC and CD, several infertility treatment characteristics were associated with achieving a live birth. Patients without a live birth underwent more cycles than patients who did achieve a live birth among both UC (median of 3.0 vs. 2.0, $p = 0.01$; Supplementary Table 1) and CD patients (median of 3.0 vs. 1.0, $p = 0.002$; Supplementary Table 2). Similarly, patients without a live birth were given a higher median dose of gonadotropins among both UC (2213 vs. 3300 IU, $p = 0.02$) and CD patients (4800 vs. 2325 IU, $p = 0.01$). Among women with UC, assisted hatching was used more frequently in patients without a

live birth compared to patients with a live birth (36.4 vs. 8.3 %, $p = 0.01$); there was no difference among women with CD ($p = .57$). For both patients with UC and CD, peak estradiol level, the use of intracytoplasmic sperm injection, and the number of embryos cryopreserved did not differ between women who did and did not achieve a live birth.

Discussion

We previously demonstrated that women with UC and CD achieve similar rates of live birth following IVF as the general infertility population [9, 10]. In this study, we further examined the association of several demographic, infertility and IBD characteristics with live birth. As expected, based on data from the general infertility population, younger age, lower dose of gonadotropins, and fewer cycles were associated with achievement of live birth in both UC and CD patients. Lower BMI and lower levels of CD3 FSH were associated with live birth among CD patients, while the use of assisted hatching was associated with unsuccessful IVF among UC patients.

Length of UC diagnosis was associated with IVF success in that patients with UC who did not achieve live birth had a longer median duration of diagnosis compared with those who achieved live birth. As age was unrelated to duration of UC diagnosis, it is unclear why this would affect live birth. Duration of diagnosis was not associated with live birth among CD patients. As previously demonstrated, successful IVF was not associated with history of total proctocolectomy with IPAA [10]. This is particularly important given that UC patients with a history of IPAA are more likely to be infertile [8]. Newly demonstrated in this study, permanent ileostomy for UC was not associated with IVF success. Similarly, among patients with CD, prior IBD surgery was not associated with live birth. Although not statistically significant, there appeared to be a trend that in patients with CD, total proctocolectomy and permanent ileostomy were associated with a lower likelihood of success following IVF, though this would need to be confirmed in a larger cohort.

For patients with UC and CD, medications at the time of IVF were not associated with the achievement of live birth. Though this also was largely true for past medications, prior use of biologics in patients with UC was associated with decreased IVF success. However, this comparison was made for only three patients (0 patients in the live birth group and 3 patients in the no live birth group). With so few patients, it is difficult to draw any definitive conclusions. This was not the case for patients with CD, for whom past medications (including biologics) had no effect on the achievement of live birth.

While disease activity may play a role in the success of IVF, almost all of the patients in this study were in remission, which may be due to the general recommendation that IBD patients be in remission before becoming pregnant [11]. Among the 39 patients with UC and without IPAA who were in remission, 34 had a partial Mayo score of 0 at the time of IVF. Although our findings suggest that women with UC are more likely to achieve live birth when they have a partial Mayo score of 0, we did not observe this difference when grouping together women with a partial Mayo score of 0 or 1. These findings must be carefully interpreted given the small sample size. Additionally, retrospective calculation of the partial Mayo score is not validated. Unlike women with UC and without IPAA, disease activity in patients with

an IPAA was not associated with live birth. However, this assertion must again be interpreted with caution given the small sample size and extent of missing data for disease activity. The categorization of patients as active versus inactive was not based on a standardized disease activity scale given the lack of such a tool in the literature. In addition, the index was applied retrospectively, and nearly one-third of patients in the IPAA group were missing disease activity.

Similar to the patients with UC, most patients with CD were in remission (79.5 %). Only 12.8 % of patients had mild disease, and no patients had moderate or severe disease at the time of IVF. Although disease activity in patients with CD did not appear to be associated with IVF outcome, again, these data must be interpreted with caution due to limitations noted above.

There are several limitations of the study, including its retrospective nature and the inclusion of patients from large tertiary care centers, which may somewhat limit the generalizability of the findings. Additionally, many patients were not on medications at the time of IVF. Some of this may be explained by the fact that over one-third of the UC patients had already undergone total proctocolectomy and IPAA or ileostomy and therefore did not require medications at the time of IVF. Similarly, over half of CD patients had undergone surgery, which may account for fewer patients being on medications at the time of IVF. Furthermore, some women who are attempting to become pregnant will self-discontinue medications due to personal concerns of teratogenicity, which may explain the lower-than-expected number of patients on medications at the time of IVF. Finally, as previously mentioned, a significant limitation of this study was the retrospective calculation of disease activity for both UC and CD. Although these scoring systems were calculated and applied after intensive chart review, the accuracy of the ultimate score assigned may be limited, especially with sub-scores such as “physician's global assessment” in the partial Mayo score and “overall general well-being” in the HBI. In addition, most patients were categorized as being in remission, which limits our ability to assess differences in IVF outcomes among patients with varying disease activity indices. This is likely a reflection of the recommendation that patients' IBD be in remission before becoming pregnant and the fact that this highly motivated patient population undergoing IVF is likely to heed this advice. Furthermore, our results must be interpreted with caution due to the small sample sizes and thus limited power, as well as the extent of missing data for determining disease activity.

We have shown that, as may be expected, age and BMI are associated with successful IVF. Though the length of disease and possibly disease activity in patients with UC may also be associated with live birth, further study is needed to confirm these results. We would continue, however, to recommend that patients with IBD be in remission before attempting IVF, similar to recommendations that patients be in remission prior to getting pregnant. It is important to note that prior surgical treatment and current medications in both UC and CD did not appear to be associated with the success of IVF. Clinically, this information is relevant to practitioners and patients when discussing medical and surgical treatment of IBD and the potential success of IVF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Narri SR, Ahn C, Buchman A. Voluntary childlessness is increased in women with inflammatory bowel disease. *Inflamm Bowel Dis*. 2007; 13:591–599. [PubMed: 17206690]
2. Manosa M, Navarro-Llavat M, Marin L, et al. Fecundity, pregnancy outcomes and breastfeeding in patients with inflammatory bowel disease: a large cohort study. *Scand J Gastroenterol*. 2013; 48:427–432. [PubMed: 23477328]
3. Muller KR, Prosser R, Bampton P, et al. Female gender and surgery impair relationships, body image, and sexuality in inflammatory bowel disease: patient perceptions. *Inflamm Bowel Dis*. 2010; 16:657–663. [PubMed: 19714755]
4. Marin L, Manosa M, Garcia-Planella E, et al. Sexual function and patients' perceptions in inflammatory bowel disease: a case– control survey. *J Gastroenterol*. 2012; 48:713–720. [PubMed: 23124604]
5. Wikland M, Jansson I, Asztely M, et al. Gynaecological problems related to anatomical changes after conventional proctocolectomy and ileostomy. *Int J Colorectal Dis*. 1990; 5:49–52. [PubMed: 2313157]
6. Oresland T, Palmblad S, Ellstrom M, et al. Gynaecological and sexual function related to anatomical changes in the female pelvis after restorative proctocolectomy. *Int J Colorectal Dis*. 1994; 9:77–81. [PubMed: 8064194]
7. Cornish JA, Tan E, Teare J, et al. The effect of restorative proctocolectomy on sexual function, urinary function, pregnancy and delivery: a systematic review. *Dis Colon Rectum*. 2007; 50:1128–1138. [PubMed: 17588223]
8. Waljee A, Waljee J, Morr AM, et al. Threefold increased risk of infertility: a meta-analysis of infertility after ileal pouch anal anastomosis in ulcerative colitis. *Gut*. 2006; 55:1575–1580. [PubMed: 16772310]
9. Oza SS, Pabby V, Dodge LE, et al. In vitro fertilization in women with inflammatory bowel disease is as successful as in women from the general infertility population. *Clin Gastroenterol Hepatol*. 2015; 13:1641–1646. [PubMed: 25818081]
10. Pabby V, Oza SS, Dodge LE, et al. In vitro fertilization is successful in women with ulcerative colitis and ileal pouch anal anastomosis. *Am J Gastroenterol*. 2015; 110:792–797. [PubMed: 25512339]
11. Abhyankar A, Ham M, Moss AC. Meta-analysis: the impact of disease activity at conception on disease activity during pregnancy in patients with inflammatory bowel disease. *Aliment Pharmacol Ther*. 2013; 38:460–466. [PubMed: 23855477]

Abbreviations

BMI	Body mass index
CD	Crohn's disease
IVF	In vitro fertilization
IBD	Inflammatory bowel disease
IQR	Interquartile range
UC	Ulcerative colitis
CD3 FSH	Cycle day three follicle-stimulating hormone

BIDMC	Beth Israel Deaconess Medical Center
BWH	Brigham and Women's Hospital
HBI	Harvey–Bradshaw Index
IPAA	Ileal pouch anal anastomosis

Table 1
Characteristics of ulcerative colitis patients at first cycle, overall and stratified by whether live birth was achieved by the end of up to six IVF cycles

Characteristic	All ulcerative colitis <i>N</i> = 71	Live birth <i>N</i> = 49	No live birth <i>N</i> = 22	<i>P</i> *
Age (years)	35.1 (32.6–39.0)	34.1 (32.4–37.8)	37.7 (33.4–40.3)	0.03
Body mass index	22.9 (21.0–25.0)	22.5 (21.0–24.2)	24.0 (22.4–27.8)	0.06
Parity— <i>n</i> (%)				0.31
0	49 (69.0)	32 (65.3)	17 (77.3)	
1+	22 (31.0)	17 (34.7)	5 (22.7)	
Cycle day three follicle-stimulating hormone (mIU/ml)	7.0 (6.0–9.1)	6.8 (5.9–8.7)	7.5 (6.3–9.9)	0.34
Infertility diagnosis— <i>n</i> (%)**				
Male factor	18 (25.7)	15 (31.3)	3 (13.6)	0.12
Tubal factor	16 (22.9)	10 (20.8)	6 (27.3)	0.55
Ovulatory dysfunction	8 (11.4)	5 (10.4)	3 (13.6)	0.70
Endometriosis	2 (2.9)	2 (4.2)	0 (0.0)	1.00
Diminished ovarian reserve	3 (4.3)	2 (4.2)	1 (4.6)	1.00
Uterine factor	2 (2.9)	1 (2.1)	1 (4.6)	0.53
Unexplained	23 (32.9)	15 (31.3)	8 (36.4)	0.67
Missing	4 (5.6)	3 (12.5)	1 (2.1)	0.11

Data are presented as the median and interquartile range except where noted

* *P* value is comparing those who achieved a live birth by the end of treatment with those who did achieve a live birth by the end of treatment

** One patient was missing infertility diagnosis, so the denominator is 70

Table 2
Characteristics of Crohn's disease patients at first cycle, overall and stratified by whether live birth was achieved by the end of up to six IVF cycles

Characteristic	All Crohn's disease <i>N</i> = 49	Live birth <i>N</i> = 28	No live birth <i>N</i> = 21	<i>P</i> *
Age (years)	35.4 (32.0–39.1)	32.3 (30.5–36.1)	39.1 (35.4–41.2)	<0.001
Body mass index	23.0 (21.6–26.0)	21.8 (21.0–24.0)	25.0 (22.5–28.0)	0.02
Parity— <i>n</i> (%)				0.52
0	35 (71.4)	19 (67.9)	16 (76.2)	
1+	14 (28.6)	9 (32.1)	5 (23.8)	
Cycle day three follicle-stimulating hormone (mIU/ml)	7.0 (6.0–9.0)	6.6 (6.0–8.0)	9.1 (6.0–11.2)	0.02
Infertility diagnosis— <i>n</i> (%)				
Male factor	7 (14.3)	5 (17.9)	2 (9.5)	0.68
Tubal factor	12 (24.5)	9 (32.1)	3 (14.3)	0.15
Ovulatory dysfunction	5 (10.2)	3 (10.7)	2 (9.5)	1.00
Endometriosis	1 (2.0)	0 (0.0)	1 (4.8)	0.43
Diminished ovarian reserve	3 (6.1)	0 (0.0)	3 (14.3)	0.07
Uterine factor	1 (2.0)	0 (0.0)	1 (4.8)	0.43
Unexplained	13 (26.5)	7 (25.0)	6 (28.6)	0.78
Missing	6 (12.2)	2 (7.1)	4 (19.1)	0.38

Data are presented as the median and interquartile range except where noted

* *P* value is comparing those who achieved a live birth by the end of treatment with those who did achieve a live birth by the end of treatment

Table 3
Disease characteristics of patients with ulcerative colitis, overall and stratified by whether live birth was achieved by the end of up to six IVF cycles

Characteristic	Ulcerative colitis <i>N</i> = 71	Live birth <i>N</i> = 49	No live birth <i>N</i> = 22	<i>P</i> *
Length of diagnosis (years)—median (IQR)	8.9 (4.6–15.0)	6.7 (4.2–9.5)	14.8 (11.0–17.6)	<0.001
Partial Mayo score at time of IVF [†]				
0	34 (73.9)	28 (82.4)	6 (50.0)	0.03
1	5 (10.9)	2 (5.9)	3 (25.0)	0.10
2	4 (8.7)	3 (8.8)	1 (8.3)	1.00
3	2 (4.3)	1 (2.9)	1 (8.3)	0.46
Unknown	1 (2.2)	0 (0.0)	1 (8.3)	0.26
Surgical treatment(s)	29 (40.9)	18 (36.7)	11 (50.0)	0.31
Colectomy and IPAA	22 (31.0)	14 (28.6)	8 (36.4)	0.51
Total proctocolectomy with permanent ileostomy	3 (4.2)	2 (4.1)	1 (4.5)	0.17
History of gynecologic surgeries	10 (14.1)	6 (13.6)	4 (20.0)	0.49
Current medications [‡]				
Oral 5-ASA	21 (34.4)	12 (28.6)	9 (47.4)	0.15
Topical/suppository 5-ASA	5 (8.2)	5 (11.9)	0 (0.0)	0.31
Topical/suppository steroid	5 (8.2)	3 (7.1)	2 (10.5)	0.64
Antibiotics	0 (0.0)	0 (0.0)	0 (0.0)	–
Conventional glucocorticoids	1 (1.6)	0 (0.0)	1 (5.3)	0.13
Non-systemic glucocorticoids	0 (0.0)	0 (0.0)	0 (0.0)	–
Immunomodulators	5 (8.3)	4 (9.8)	1 (5.3)	0.57
Biologics	1 (1.6)	0 (0.0)	1 (5.3)	0.13
Methotrexate	0 (0.0)	0 (0.0)	0 (0.0)	–
Past medications				
Oral 5-ASA	41 (57.7)	28 (57.1)	13 (59.1)	0.88
Topical/suppository 5-ASA	22 (31.0)	16 (32.7)	6 (27.3)	0.78
Topical/suppository steroid	16 (22.5)	10 (20.4)	6 (27.3)	0.55
Antibiotics	9 (12.7)	5 (10.2)	4 (18.1)	0.44
Conventional glucocorticoids	23 (32.4)	15 (30.6)	8 (36.4)	0.63
Non-systemic glucocorticoids	0 (0.0)	0 (0.0)	0 (0.0)	–
Immunomodulators	10 (14.1)	6 (12.2)	4 (18.2)	0.49
Biologics	3 (4.2)	0 (0.0)	3 (13.6)	0.03
Methotrexate	1 (1.4)	0 (0.0)	1 (4.6)	0.31
Disease activity among IPAA patients at time of IVF [§]	<i>N</i> = 22	<i>N</i> = 14	<i>N</i> = 8	0.78
Active	4 (18.2)	2 (14.3)	2 (25.0)	0.48
Inactive	11 (50.0)	7 (50.0)	4 (50.0)	1.00
Unknown	7 (31.8)	5 (35.7)	2 (25.0)	0.60

Data are presented as *n* (%) except where noted

IQR interquartile range, *IPAA* ileoanal pullthrough, *GYN* gynecologic, *ASA* aminosalicylic acid

* *P* value is comparing those who achieved a live birth by the end of up to six IVF cycles with those who did achieve a live birth by the end of up to six IVF cycles

† Excludes 25 patients with IPAA/TPC where the partial Mayo score is not applicable; thus, the denominator is 46; the denominators for live birth and no live birth are 34 and 12, respectively

‡ Patients may be on more than one current medication; 11 patients were missing information on current use of immunomodulators; thus, the denominator is 60; 10 patients were missing information on all other current medications; thus, the denominator is 61 (denominators for immunomodulators are 41 in live birth and 19 in no live birth; denominators for all other current medications are 42 in live birth and 19 in no live birth)

§ Includes only 22 patients with IPAA; the denominator for all UC patients is 22, the denominator for live birth is 14, and the denominator for no live birth is 8

Table 4
Disease characteristics of patients with Crohn's disease, overall and stratified by whether live birth was achieved by the end of up to six IVF cycles

Characteristic	Crohn's disease <i>N</i> = 49	Live birth <i>N</i> = 28	No live birth <i>N</i> = 21	<i>P</i> *
Length of diagnosis (years)—median (IQR)	10.3 (5.6–16.1)	9.0 (5.6–15.4)	10.7 (5.1–21.9)	0.41
Harvey–Bradshaw Index at time of IVF [†]				
Remission	31 (79.5)	20 (83.3)	11 (73.3)	0.69
Mild	5 (12.8)	2 (8.3)	3 (20.0)	0.35
Unknown	3 (7.7)	2 (8.3)	1 (6.7)	1.00
Surgical treatment(s)	26 (53.1)	14 (50.0)	12 (70.6)	0.62
Ileocecal resection	9 (18.4)	6 (21.4)	3 (14.3)	0.71
Strictureplasty	1 (2.0)	1 (3.6)	0 (0.0)	1.00
Right hemicolectomy	0 (0.0)	0 (0.0)	0 (0.0)	–
Left hemicolectomy	1 (2.0)	0 (0.0)	1 (4.8)	0.43
Colectomy and IPAA	1 (2.0)	1 (3.7)	0 (0.0)	1.00
Total proctocolectomy with permanent ileostomy	8 (16.3)	2 (7.1)	6 (28.6)	0.06
Diverting ostomy	1 (2.0)	1 (3.6)	0 (0.0)	1.00
Small intestinal resection	11 (22.4)	9 (32.1)	2 (9.5)	0.09
History of gynecologic surgeries	6 (12.2)	3 (10.7)	3 (14.3)	1.00
Current medications [‡]				
Oral 5-ASA	14 (32.6)	9 (34.6)	5 (29.4)	0.72
Topical/suppository 5-ASA	0 (0.0)	0 (0.0)	0 (0.0)	–
Topical/suppository steroid	0 (0.0)	0 (0.0)	0 (0.0)	–
Antibiotics	1 (2.3)	0 (0.0)	1 (5.9)	0.21
Conventional glucocorticoids	2 (4.7)	2 (7.7)	0 (0.0)	0.24
Non-systemic glucocorticoids	1 (2.3)	0 (0.0)	1 (5.9)	0.21
Immunomodulators	2 (4.7)	1 (3.8)	1 (5.9)	0.76
Biologics	4 (9.3)	3 (11.5)	1 (5.9)	0.53
Methotrexate	0 (0.0)	0 (0.0)	0 (0.0)	–
Past medications				
Oral 5-ASA	30 (61.2)	19 (67.9)	11 (52.4)	0.27
Topical/suppository 5-ASA	3 (6.1)	2 (7.1)	1 (4.2)	1.00
Topical/suppository steroid	2 (4.1)	2 (7.1)	0 (0.0)	0.50
Antibiotics	14 (28.6)	7 (25.0)	7 (33.3)	0.52
Conventional glucocorticoids	21 (42.9)	13 (46.4)	8 (38.1)	0.56
Non-systemic glucocorticoids	1 (2.0)	0 (0.0)	1 (4.8)	0.43
Immunomodulators	12 (24.5)	4 (14.3)	8 (38.1)	0.06
Biologics	8 (16.3)	4 (14.3)	4 (19.1)	0.71
Methotrexate	1 (2.0)	0 (0.0)	1 (4.8)	0.43

Data are presented as *n* (%) except where noted

IQR interquartile range, *IPAA* ileoanal pullthrough, *GYN* gynecologic, *ASA* aminosalicilic acid

* P value is comparing those who achieved a live birth by the end of treatment with those who did achieve a live birth by the end of treatment

† Excludes 1 patient with IPAA, one patient with diverting ostomy, and eight patients with total proctocolectomy with permanent ileostomy where the Harvey–Bradshaw Index is not applicable; thus, the denominator is 39; the denominators for live birth and no live birth are 24 and 15, respectively

‡ Patients may be on more than one current medication; six patients were missing information on current medications; thus, the overall denominator is 43; the denominators for live birth and no live birth are 26 and 17, respectively