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# The impact of pregnancy on surgical Crohn disease: an analysis of the Nationwide Inpatient Sample



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## ABSTRACT

**Background:** The impact of pregnancy on the course of Crohn disease is largely unknown. Retrospective surveys have suggested a variable effect, but there are limited population-based clinical data. We hypothesized pregnant women with Crohn disease will have similar rates of surgical disease as a nonpregnant Crohn disease cohort.

**Material and methods:** International Classification of Diseases, Ninth Revision, Clinical Modification codes were used to identify female Crohn patients from all patients admitted using the Nationwide Inpatient Sample (1998–2009). Women were stratified as either pregnant or nonpregnant. We defined Crohn-related surgical disease as peritonitis, gastrointestinal hemorrhage, intra-abdominal abscess, toxic colitis, anorectal suppuration, intestinal–intestinal fistulas, intestinal–genitourinary fistulas, obstruction and/or stricture, or perforation (excluding appendicitis).

**Results:** Of the 92,335 women admitted with a primary Crohn-related diagnosis, 265 (0.3%) were pregnant. Pregnant patients were younger (29 versus 44 y;  $P < 0.001$ ) and had lower rates of tobacco use (6% versus 13%;  $P < 0.001$ ). Pregnant women with Crohn disease had higher rates of intestinal–genitourinary fistulas (23.4% versus 3.0%;  $P < 0.001$ ), anorectal suppuration (21.1% versus 4.1%;  $P < 0.001$ ), and overall surgical disease (59.6% versus 39.2%;  $P < 0.001$ ). On multivariate logistic regression analysis controlling for malnutrition, smoking, age, and prednisone use, pregnancy was independently associated with higher rates of anorectal suppuration (odds ratio [OR], 5.2; 95% confidence interval [CI], 3.8–7.0;  $P < 0.001$ ), intestinal–genitourinary fistulas (OR, 10.4; 95% CI, 7.8–13.8;  $P < 0.001$ ), and overall surgical disease (OR, 2.9; 95% CI, 2.3–3.7;  $P < 0.001$ ).

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**Conclusions:** Pregnancy in women with Crohn disease is a significant risk factor for Crohn-related surgical disease, in particular, anorectal suppuration and intestinal–genitourinary fistulas.

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## 1. Introduction

Crohn disease (CD) classically has a bimodal age distribution [1], and for those afflicted, this often includes reproductive-age women. Although many of these women may choose not to conceive [2], those with quiescent CD are considered to be as likely to become pregnant as the general population [3–5]. In fact, it has been estimated that 25% of women with known inflammatory bowel disease will conceive [6]. As such, obstetricians, gastroenterologists, and surgeons not infrequently find themselves caring for and advising pregnant patients who carry the burden of Crohn disease.

Unfortunately, little evidence exists to help guide clinical decision making and counseling regarding the course of CD in pregnant patients. The general consensus is that pregnant patients are as likely to flare during pregnancy as they are in a nonpregnant state [7], with rates ranging from 26%–34% [7–9]. In practice, patients are often counseled that one-third of CD patients who conceive while in remission will relapse during pregnancy, and two-thirds of CD patients who conceive in the face of active disease will smolder or deteriorate [6,11]. Still, many clinicians feel that pregnancy may actually improve disease activity, presumably secondary to a state of relative immune-suppression [10]. Although this lack of consensus on the clinical course of CD during pregnancy is likely because of the unique experience of individual centers caring for these patients, it is also based on limited, and low volume, levels III and IV evidence. Furthermore, few studies address the severity of disease activity or the frequency of Crohn-related surgical disease in the pregnant Crohn patient.

We therefore sought to assess the impact of pregnancy on severity of CD using Crohn-related surgical disease as a surrogate for severe disease activity. We hypothesized that pregnant women with CD would have similar rates of surgical disease as a nonpregnant CD cohort.

## 2. Materials and methods

After approval by our local Institutional Review Board, we performed a population-based retrospective review of all women who were admitted with a diagnosis of Crohn disease between 1998 and 2009, as reported to the Nationwide Inpatient Sample (NIS). The NIS is composed of de-identified Health Insurance Portability and Accountability Act-compliant data from >1000 hospitals and >8 million admissions annually across the United States. The data is gathered and submitted by Health Care Cost and Utilization Project partners, which are state data organizations that have partnered with the Agency for Healthcare Research and Quality. It provides information on primary and secondary diagnoses, primary and secondary procedures, admission and discharge status (to include mortality), patient demographics, total charges, and length of stay.

Demographic information included variables such as age, area of CD involvement, smoking history, nutrition status, and pregnancy status. The primary outcome of interest was Crohn-related surgical disease, which we defined as the presence of peritonitis, gastrointestinal hemorrhage, intra-abdominal abscess, toxic colitis, anorectal suppuration, intestinal–intestinal fistulas, intestinal–genitourinary fistulas, obstruction and/or stricture, or perforation. To limit potential confounders, only women were included in this study. Women meeting inclusion criteria were identified by *International Classification of Diseases, Ninth Revision* codes. These included 555.0 (small bowel regional enteritis), 555.1 (large bowel regional enteritis), 555.2 (small and large bowel regional enteritis), and 555.9 (unspecified regional enteritis). We further narrowed our study population by including only women with a primary diagnosis of either CD itself or a secondary diagnosis of CD with a primary diagnosis of CD-related surgical disease (Fig.; Supplement A). Exclusion criteria included non-CD-related diagnoses that can present with an acute abdomen (Supplement B). The study group was then stratified as either pregnant or nonpregnant (Supplement C).

Pregnant and nonpregnant women with CD were then compared in terms of demographics (age [linear], smoking status [V15.82], presence of malnutrition [260–269.9], ongoing chronic steroid use [V58.65], region of Crohn involvement [small bowel, large bowel, combined, and nonspecific], and presence of surgical disease [peritonitis, gastrointestinal hemorrhage, intra-abdominal abscess, toxic colitis, anorectal suppuration, intestinal–intestinal fistulas, intestinal–genitourinary fistulas, obstruction and/or stricture, or perforation]).

### 2.1. Statistical analysis

Descriptive and univariate analyses were performed using chi-square or Student *t*-tests. Multivariate logistic regression analyses were performed to adjust for any disparities between the study groups and to identify independent contributors to surgical disease. Dependent variables of interest included anorectal suppuration (abscess and/or fistula), intestinal–genitourinary fistulas, bowel obstruction and/or stricture, and overall surgical disease (peritonitis, gastrointestinal hemorrhage, intra-abdominal abscess, toxic colitis, anorectal suppuration, intestinal–intestinal fistulas, intestinal–genitourinary fistulas, obstruction, or perforation). Independent variables of interest included age (linear), smoking status, pregnancy, malnutrition, and ongoing chronic steroid use. Hospital size, region, rural setting, and teaching institution were controlled for in our multivariate analyses. Logistic regression results are presented as odds ratio with 95% confidence interval. Statistical analyses were performed using PASW Statistics 18.0 (SPSS Inc, Chicago, IL), and significance was set at  $P < 0.05$ .

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