American Journal of Gastroenterology and Hepatology

ISSN 2692-7942

Research Article

Management of Inflammatory Bowel Disease during Pregnancy amongst Healthcare Professionals in Florida: A Cross-Sectional Survey

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Abstract

Inflammatory Bowel Disease (IBD) poses a significant global health concern, with a rising incidence particularly among women of reproductive age. Managing IBD during family-planning, pregnancy, and post-partum periods presents complex challenges. This study aims to quantify prevalent practices in IBD management among pregnant patients, comparing academic *vs.* community settings, and gastroenterologist's *vs.* obstetricians or advanced practice providers. An internet-based cross-sectional survey assessed knowledge and practices among 105 respondents, with 63% gastroenterologists, 21% advanced practice providers, 7% obstetricians, and others across community and academic settings. While most reported feeling comfortable managing IBD, medication management was variable. 75.3% and 78.7% reported continuing oral and topical aminosalicylates respectively, 39% reported continuing oral corticosteroids, and 92.8% reported discontinuing methotrexate at conception with variable statistical significance amongst type of provider. Management of immunomodulators revealed inconsistencies without notable significance comparing gastroenterologist's *vs.* other healthcare professionals. However, most gastroenterologists favored continuing most biologics, significantly more than other providers. Many respondents (54% and 71.1% respectively) felt gastroenterologists should counsel on preconception and modify medications accordingly during pregnancy. This study underscores the need for enhanced preconception counseling and education, standardizing the management of pregnant IBD patients. Discrepancies in medication usages emphasize the importance of ongoing medical education for all healthcare providers, especially with ever-changing and newly available therapies. While limitations include a small respondent pool, the study highlights significant gaps in knowledge and practices, emphasizing the urgency for broader studies and educational initiatives to ensure exceptional care for pregnant IBD patients.

Keywords: IBD; Crohn's disease; Ulcerative colitis; Pregnant; Pregnancy

Introduction

Inflammatory Bowel Disease (IBD) stands as a global health concern, affecting an estimated 7 million individuals worldwide as of 2017. Among these, approximately 3.1 million are adults in the United States, with the incidence of new diagnoses steadily rising [1-3]. Nearly half of these cases involve women, a large proportion of which will either develop or carry the diagnosis during their reproductive years. Although Crohn's Disease (CD) and Ulcerative Colitis (UC) can manifest at any stage of life, the majority of diagnoses occur between ages 15 and 35, with a bimodal incidence peak later in life [3,4].

Managing these complex disease processes demands comprehensive care and often necessitates multidisciplinary input at any phase or age within the disease trajectory. However, the intricacies notably amplify when considering family planning, pregnancy, and post-partum care. Patients grappling with ongoing symptoms and flares, apprehensions regarding genetic predisposition in their child, potential risks of IBD-related congenital abnormalities, medication teratogenicity, or receiving advice from healthcare providers that conception may be inadvisable or unfeasible might choose voluntary infertility [5]. In fact, voluntary childlessness may be accentuated in IBD patients, influencing pregnancy rates with estimates ranging from 17% to 44% [6,7]. Thus, psychosocial factors, including disease awareness, should be incorporated into discussions surrounding fertility. Notably, infertility rates among IBD patients with quiescent disease or lack of specific surgical history align with rates in the general population [8-10]. Among those planning or experiencing pregnancy, risks of adverse outcomes such as miscarriage, Small for Gestational Age (SGA) infants, preterm delivery, Preterm Pre-labor Rupture of Membranes (PPROM), and emergent caesarean deliveries are heightened [7-9,11,12]. Additionally, the impact of IBD on maternal health, along with concerns about ongoing medication use as it relates to both side effects and compliance that must be discussed between patient and provider [13,14].

Preconception counseling and awareness play a vital role for future mothers and healthcare providers, necessitating an understanding of the effects of IBD during pregnancy, including appropriate therapeutic strategies [7]. These uncertainties can be mitigated by the involvement of a multidisciplinary team from pre-conception through the post-partum period, but there remains great variability in the management practices in the care of this patient population

Citation: Gosnell H, Narayanan S, Mendoza S, Chaphalkar C, Kumar A, Seminerio J. Management of Inflammatory Bowel Disease during Pregnancy amongst Healthcare Professionals in Florida: A Cross-Sectional Survey. Am J Gastroenterol Hepatol. 2024;5(1):1026.

Publisher Name: Medtext Publications LLC

Manuscript compiled: Apr 12th, 2024

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[14]. Thus, this study's aim is to quantify the prevalent practices of IBD management amongst pregnant patients, and in the peri- and post-partum periods. We further seek to compare practice patterns in academic *vs.* community settings, and those of gastroenterologists and obstetricians as compared to advanced practice providers in their fields.

Materials and Methods

Study design

We performed an internet-based cross-sectional survey study. We aimed to assess knowledge and practice patterns in the management of patients with IBD in the pre-conception, pregnancy, and post-partum periods among gastroenterology and obstetrics providers. The study was performed and reported following the Checklist for Reporting Results of Internet E-Surveys guidelines [15].

Setting

The study was accessible to gastroenterology and obstetrics providers *via* the Florida Gastroenterological Society, as well as the USF Health Inflammatory Bowel Disease Center between January 2021 through June 2022.

Survey measures

The survey's contents were designed by the authors of the present study. The design of the survey was informally validated at the senior authors' institution. The faculty authors reviewed the survey after development, with necessary changes made. The study did not undergo any formal validation.

Access to the survey was available *via* a URL and a QR code distributed by email and in person, respectively, through the Florida Gastroenterological Society as well as the USF Health Inflammatory Bowel Disease Center. Completion was voluntary and not incentivized. The 27-item questionnaire entailed questions regarding provider demographics, subjective comfort and knowledge about IBD management, and an objective assessment of provider knowledge surrounding management of medical therapies during the pre-conception through post-partum periods. Of the 27 questions, 10 evaluated provider and practice demographics, five assessed subjective knowledge and comfort in IBD management, six assessed practice patterns, two assessed patient behaviors, and three provided an objective assessment of provider knowledge. Item formats included yes/no questions, 4- and 5-point Likert scales, and demographic information (e.g. specialty, practice setting, provider type, and clinical experience). The survey questions used in this study are shown in the Appendix.

Survey administration

Between January 2021 and June 2022, the survey was distributed *via* E-mail and in person to gastroenterology and obstetrics providers through the Florida Gastroenterological Society as well as the USF Health Inflammatory Bowel Disease Center. Multiple emails were sent *via* listserv, wherein providers were given both a URL and a QR code to access the survey. The length of the survey administration period was extended to optimize in person survey access though society meetings and allow sufficient response time. Those who answered at least the first question were considered respondents. All surveys were included in the analysis. Unique survey views and participation rate were not tracked. No unique user identifier was assigned to each client or computer. No cookies, data regarding the IP address of a client computer, or other techniques were used to track participation.

The institutional review board at the senior author's institution approved the study. Participants received informed consent before initiating the anonymous survey. Participants were told of the study's purpose, which the investigator is, the survey length, and which data were stored, where, and for how long. No personal information was collected or stored.

Results

Survey respondents included 63% practicing gastroenterologists, 13% nurse practitioners, 8% physician assistants, 7% obstetrics/gynecologists, 5% gastroenterology trainees and 4% other health professionals. Many respondents were either early in their career with length of practice <5 years (33%) or later in their career with over 20 years of experience (29%), primarily practicing in a private outpatient setting (43.6%) as opposed to a clinical academic hospital (31.7%). A total of 22.8% reported working primarily at a community hospital. Majority of clinicians (45%) report seeing <10% IBD patients in their panel and 40% reported seeing 10% to 25% of IBD patients.

Specifically managing and following patients with IBD during their pregnancy was more limited. Sixty-two percent (62%) of providers reported treating 1-10 pregnant IBD patients and 27% reported not treating any IBD patient during pregnancy within the last year. Overall, only 19% felt they had "very good" knowledge base regarding IBD therapies, let alone feel "extremely comfortable" managing IBD patients during a pregnancy (6%). When comparing self-reported confidence in IBD therapies and managing patients during pregnancy there was no significant difference found when comparing physicians to other health care professionals (p-values 0.404 and 0.357, respectively). Many participants (32%) reported feeling somewhat comfortable managing pregnant IBD patients, with nearly half (56%) of the clinicians routinely discussing family planning with patients. Thirty-nine percent (39%) of the participants reported that very few (<10%) of their patients provided information about attempts to conceive. In terms of medications used during pregnancy, 75.3% of all respondents reported continuation of mesalamine/sulfasalazine and 78.7% reported continue of mesalamine topicals such as mesalamine enemas and suppositories. Of these, 63.4% were physicians, and 11.8% were other healthcare professionals, who would choose to continue this medication. There was a significant difference in the management of oral mesalamine and topical mesalamine when comparing gastroenterologists to other healthcare professionals (p-value 0.015 and 0.010, respectively).

Regarding oral steroids, thirty-nine percent (39%) of all respondents would continue prednisone dose unchanged while 27.7% would stop prednisone administration altogether. Of those continuing steroids, 35.1% were physicians while only 4.3% were other healthcare professionals; this was statistically significant (p-value 0.006). On the contrary, 54.8% of all providers would continue the use of oral budesonide formulation unchanged and topical steroid-based foam formulations (72.6%). Of these, 48.4% of physicians and 6.5% of other healthcare professionals would continue oral budesonide unchanged, showing significant differences in managements between the two groups (p-value 0.003). Many providers (92.8%) discontinued methotrexate at the time of conception, but 5.2% of respondents were unsure about this medication, with 2.1% of physicians opting to continue the methotrexate. Of these, 72% of all physicians would discontinue methotrexate, as opposed to 20.6% of all healthcare professionals who would choose to discontinue as well. There was no statistical significance in management of methotrexate between

gastroenterologists *vs.* other health professionals (p-value 0.112).

Respondents were less clear about management of immunomodulators during time of conception. Azathioprine discontinuation during pregnancy was found to be done by 43% of all providers, and 40% would continue the medication with unchanged dosing during pregnancy. There was no statistical difference between the management of azathioprine when comparing physicians to other health professionals (p-value 0.057). Forty-six percent (46%) of all providers would discontinue tacrolimus and 38.9% reported feeling unsure about this medication during pregnancy. A small proportion of physicians (11.6%) would continue tacrolimus. There was no significant difference in management between physicians and other healthcare professionals (p-value 0.445). In terms of biologics, the majority would have continued therapy with infliximab (79.2%), adalimumab (81.3%), certolizumab (76.6%), golimumab (67.4%), ustekinumab (76.2%) and vedolizumab (76.8%). However, continuation of these biologics during pregnancy differed between gastroenterologists *vs.* other healthcare professionals (p-value=0.015, 0.032, 0.024, 0.006, 0.000 respectively). Small molecule drugs like tofacitinib and ozanimod, posed a higher degree of uncertainty. Thirty-six percent (36%) chose to discontinue tofacitinib during pregnancy, but 41.5% were unsure how to proceed with the medication. Of all respondents, twenty-six (26%) percent opted to discontinue ozanimod. The majority (52%) were unsure on how to manage ozanimod in the setting of pregnancy. A total of 60 respondents chose to skip this question to avoid answering, perhaps due to high degree of uncertainty. There were no differences in responses when comparing gastroenterologists to other health professionals (p-value 0.305). Similarly, 65% of survey respondents could not answer when they would consider stopping medications depending on the trimester of pregnancy. Female IBD patients were most likely to disclose that they were trying to conceive primarily to their gastroenterologist, when compared to other healthcare professionals including nurse practitioners, physician assistants, and trainees (p-value 0.003), but no difference was found to who they decided to inform once pregnant (p-value 0.065).

When comparing all providers who responded to this survey, 64% were in private practice and 30% were working in academic institutions. There was no statistical significance in the degree of confidence on the knowledge regarding IBD therapies between these two groups (p-value 0.267). There was no difference in the management of sulfasalazine/mesalamine, prednisone, oral budesonide, topical steroid foams, topical mesalamine, and methotrexate. Azathioprine was most likely to be discontinued by a private gastroenterologist when compared to academic physicians (p-value 0.020). There was no difference in the management of tacrolimus, adalimumab, certolizumab, vedolizumab, tofacitinib, ustekinumab, ozanimod, whether managed by a private or academic gastroenterologist (Tables 1 and 2). Fifty-four percent (54%) of respondents felt that it was the gastroenterologist's responsibility to counsel during the time of preconception, with 71.7% thinking that the gastroenterologist should be in charge of modifying or discontinuing medications during pregnancy. Forty-five percent (45%) stated that they were comfortable discussing delivery options such as vaginal or cesarian delivery. However, the majority (46.9%) did not feel comfortable discussing immunizations for babies with intrauterine exposure to biologics.

Discussion

Female patients with IBD often require continuation of maintenance therapies during pregnancy. The impact of active IBD on pregnancy-related complications is well-documented. Additionally, the activity of IBD at conception plays a significant role on the rates of relapsing disease during pregnancy, as well as the risk it can inflict on the growing fetus leading to miscarriage, SGA infants, preterm labor and PPROM [7]. Drugs available for the treatment of IBD are rapidly evolving and may represent a challenge in patient care, specifically during pregnancy. This is due to lack of knowledge, changing paradigms and a rapidly evolving field [16-18]. Registries such Organization of Teratology Information Specialists (OTIS) and Pregnancy Inflammatory Bowel Disease and Neonatal Outcomes (PIANO) exist to expand our knowledge and understanding of medication safety [11,16,17]. Continued medical education for the physician and allied health professionals remains pivotal in the face of new pharmacological advances. Among currently available IBD therapies, there is a consensus categorizing medications as generally acceptable in pregnancy, those known to be teratogenic, and those where information is still lacking. While this survey captured prevalent IBD therapies, the emergence of newer options post-survey, including rizankizumab, upadacitinib, etrasimod, and mirikizumab, were not included in this study. Of those medications investigated, classes considered safe during pregnancy and breastfeeding include aminosalicylates (Mesalamine, Sulfasalzine, Balsalazide, and Olsalazine), corticosteroids, thiopurine analog, calcineurin inhibitors (Cyclosporine, Tacrolimus), anti-TNF agents (infliximab, adalimumab, olimumab, and certolizumab-pegol), anti-integrins (vedolizumab) and anti-IL12/23 inhibitors (ustekinumab). However, ozanimod and tofacitinib lack substantial data, and currently reside in an intermediate category, accompanied by label warnings [7]. Ozanimod's label indicates insufficient, well-controlled studies in pregnant patients, suggesting potential fetal harm based on animal studies, and advocates contraception during and up to three months post-treatment [19]. Tofacitinib's label suggests insufficient data on its association with major birth defects, miscarriage, or adverse maternal or fetal outcomes, highlighting risks linked to rheumatoid arthritis and UC in pregnancy [20]. Patients taking both medications can voluntarily enroll in registries for long-term risk evaluation. Methotrexate remains contraindicated in pregnancy and breastfeeding [7].

Conclusion

In this survey encompassing 105 providers, noticeable differences surfaced between gastroenterologists and other allied health professionals in their decisions regarding continuation of steroids, mesalamine and biologics during pregnancy. Discrepancies between private and academic physician practice patterns were less distinct. The advent of new small molecule therapies posed considerable challenges for many providers alike. Investigating these variations is critical given disparities between available data and actual practice. Identifying deficiencies and instituting educational initiatives to improve quality of care for pregnant patients with IBD is pivotal for long-term outcomes in this population. Pregnancy, especially within the context of chronic illness, presents formidable challenges, as these patients are often excluded from clinical trials. Thus, data collection often takes time to make accurate predictions for patient safety. Consequently, accurate safety predictions and comprehensive drug approvals for pregnant patients are delayed, creating educational gaps. Addressing these gaps requires larger-scale studies to pinpoint key areas for educational enhancement within the healthcare community.

The primary limitation of this study revolves around the small

Table 1: Survey responses to management of IBD medications during pregnancy among gastroenterologists and other providers.

Medication	Expected Answer	Gastroenterologist	Other health professional	P-values
Sulfasalazine/ Mesalamine	Continue unchanged	63.4%	11.8%	0.015
Prednisone	Continue with change in dose or frequency	19.1%	6.4%	0.006
Oral Budesonide	Continue with change in dose or frequency	15.1%	3.2%	0.003
Steroid foams (Uceris, Proctofoam)	Continue unchanged	60%	12.6%	0.068
Topical mesalamine (Canasa, Rowasa)	Continue unchanged	66%	12.8%	0.010
Methotrexate	STOP	72.2%	20.6%	0.112
Azathioprine/6MP	STOP	30.9%	12.4%	0.057
Tacrolimus (Prograf)	Continue unchanged	11.6%	1.1%	0.445
Infliximab (Remicade, Inflectra, Renflexis)	Continue unchanged	66.7%	12.5%	0.000
Adalimumab (Humira)	Continue unchanged	66.7%	14.6%	0.015
Certolizumab (Cimzia)	Continue unchanged	63.8%	12.8%	0.032
Golimumab (Simponi)	Continue unchanged	56.8%	10.5%	0.024
Vedolizumab (Entyvio)	Continue unchanged	65.3%	11.6%	0.000
Ustekinumab (Stelara)	Continue unchanged	59.5%	16.7%	0.006
Tofacitinib (Xeljanz)	STOP	26.6%	9.6%	0.305
Ozanimod (Zeposia)	STOP	19%	7.1%	0.408

Table 2: Survey responses to management of IBD medications during pregnancy among academic and private practitioners.

Medication	Expected Answer	Academic Practitioner	Private Practitioner	P-values
Sulfasalazine/ Mesalamine	Continue unchanged	0.505	0.247	0.803
Prednisone	Continue with change in dose or frequency	0.138	0.117	0.228
Oral Budesonide	Continue with change in dose or frequency	0.075	0.108	0.067
Steroid foams (Uceris/Proctofoam)	Continue unchanged	0.495	0.232	0.064
Topical mesalamine (canasa rowasa)	Continue unchanged	0.533	0.255	0.897
Methotrexate	STOP	0.608	0.32	0.714
Azathioprine/6MP	STOP	0.351	0.082	0.02
Tacrolimus (Prograf)	Continue unchanged	0.063	0.063	0.227
Infliximab (Remicade, Inflectra, Renflexis)	Continue unchanged	0.521	0.271	0.823
Adalimumab (Humira)	Continue unchanged	0.531	0.281	0.728
Certolizumab pegol (Cimzia)	Continue unchanged	0.5	0.266	0.385
Golimumab (Simponi)	Continue unchanged	0.453	0.221	0.076
Vedolizumab (Entyvio)	Continue unchanged	0.516	0.253	0.373
Ustekinumab (Stelara)	Continue unchanged	0.643	0.119	0.86319
Tofacitinib (Xeljanz)	STOP	0.223	0.138	0.899
Ozanimod (Zeposia)	STOP	0.19	0.071	0.388

population size that responded to the survey. Despite multiple online and in-person efforts, face-to-face initiatives were limited due to the COVID-19 pandemic. While our aim was to involve gastroenterology and obstetrics providers equally, disseminating the survey amongst the obstetric professionals proved challenging, resulting in few responses despite coordinated attempts to collaborate with various organizations, institutions, and practices. The majority of respondents worked in private practice, as academic institutions faced obstacles in promoting and encouraging participation. Notably, there was no incentive provided for participation. The constant addition of new medications onto the market necessitates ongoing surveillance within the gastrointestinal and obstetric communities to ensure optimal management of this patient population. This study highlights the disparities in management of the Pregnant IBD population, emphasizing the need to increase preconception counseling and ascertain whether any medication adjustments are necessary to prevent adverse outcomes.

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