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Use of Biologic Therapy by Pregnant Women With Inflammatory Bowel Disease Does Not Affect Infant Response to Vaccines

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BACKGROUND & AIMS: **In women with inflammatory bowel diseases (IBDs), exposure to immunomodulator or biologic therapy has not been associated with adverse events during pregnancy or outcomes of newborns. We investigated whether exposure of patients to these agents during pregnancy affects serologic responses to vaccines in newborns.**

METHODS: **We collected data from the Pregnancy in IBD and Neonatal Outcomes registry, which records outcomes of pregnant women with diagnosis of IBD receiving care at multiple centers in the United States, from 2007 through 2016. Serum samples collected from infants at least 7 months old were analyzed for titers of antibodies to *Haemophilus influenzae B* (HiB) or tetanus toxin; mothers completed a survey of vaccine practices and outcomes from July 2013 through October 2016. Umbilical cord blood samples from 33 infants were assayed for concentration of biologic agents. Vaccination response was compared between infants born to mothers exposed to biologic therapy (infliximab, adalimumab, certolizumab pegol, golimumab, natalizumab, vedolizumab, or ustekinumab—either as a single agent or in combination with an immunomodulator, at any time between conception and delivery) and infants born to unexposed mothers.**

RESULTS: **A total of 179 women completed the vaccine survey (26 biologic unexposed, 153 exposed to a biologic agent). We found no significant difference in proportions of infants with protective antibody titers against HiB born to exposed mothers (n = 42, 71%) vs unexposed mothers (n = 8, 50%) ($P = .41$). We also found no difference in the proportion of infants with protective antibody titers to tetanus toxoid born to exposed mothers (80%) vs unexposed mothers (75%) ($P = .66$). The median concentration of infliximab in cord blood did not differ significantly between infants with vs without protective antibody titers to HiB ($P = .30$) or tetanus toxoid ($P = .93$). Mild reactions were observed in 7/40 infants who received rotavirus vaccine and whose mothers had been exposed to biologic therapies.**

CONCLUSIONS: **Vaccination of infants against HiB and tetanus toxin, based on antibody titers measured when infants were at least 7 months old, does not appear to be affected by in utero exposure to biologic therapy.**

Keywords: Infliximab; Neonate; Immunization; Rotavirus.

Inflammatory bowel diseases (IBDs), such as Crohn's disease and ulcerative colitis, frequently affect men and women in their reproductive years. Because of the progressive, relapsing-remitting course of disease, many patients with IBD require immunosuppressive and biologic therapy to obtain disease control. Achieving and maintaining adequate disease control is important to optimize pregnancy outcomes because active disease is associated with an increase in adverse pregnancy outcomes.[1] The impact of such medications on fertility, pregnancy, and infant outcomes are of paramount importance to both the patients and the treating clinician. There have been multiple retrospective

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Abbreviations used in this paper: HiB, *Haemophilus influenzae B*; PIANO, Pregnancy in Inflammatory Bowel Disease and Neonatal Outcomes; TNF, tumor necrosis factor.

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studies that have failed to show an association between anti–tumor necrosis factor (TNF) therapy and adverse outcomes or congenital malformations in the IBD population.[2,3] However, some biologics can cross the placenta and be present in the infant for the first several months of life.[4] There are limited data on the long-term impact of this exposure on the development of the neonatal immune system. The 2010 case report of the death of an infant born to a mother on biologic therapy who was administered the Bacillus–Calmette–Guerin vaccine at 3 months remains at the forefront and drives the pursuit for continued safety in our infants born in the era of biologic therapy.[5]

Studies have quantified the anti-TNF drug concentration in the mother and infant and have shown that measurable drug concentration can persist in the infant for up to 12 months.[4,6] This persistence of drug has led to recommendations for avoiding live vaccines in infants during the time when they may have detectable concentrations of biologic drug. However, no alterations have been recommended for inactivated vaccines under the assumption that they are both safe and effective despite exposure to maternal immunosuppression. Studies in adults with IBD have shown that individuals on immunosuppression, particularly combination immunomodulator-biologic therapy, have significantly lower rates of response to inactivated vaccines including pneumococcal and influenza vaccines.[7–9] It is unknown whether an infant exposed to biologic and immunomodulator therapy in utero and/or with detectable biologic concentration in the first year of life will mount an appropriate response to inactivated vaccines.

The Pregnancy in Inflammatory Bowel Disease and Neonatal Outcomes (PIANO) registry is one of the largest prospective registries of maternal and childhood outcomes in IBD. It focuses on both pregnancy outcomes and early childhood health and development. The aims of this study were to measure infant response to vaccinations at 1 year of age and determine if maternal immunosuppression exposure affects vaccine response. In individuals in whom the serum concentration of biologic drug was available at birth, we aimed to examine if a higher drug concentration at birth was associated with an attenuated response to vaccination.

Methods

Study Cohort

The population for this study consisted of women enrolled in the Crohn's and Colitis Foundation PIANO registry, an ongoing prospective multicenter registry initiated in 2007. This prospective registry approached women with an established diagnosis of IBD receiving care at 1 of 30 centers throughout the United States. Upon obtaining informed consent, women provided detailed information regarding their demographics and characteristics of their IBD, including current and past treatments. Enrollment could occur at any point during pregnancy and participating women were followed up prospectively throughout each trimester of pregnancy, and at delivery. Children born to these mothers were followed up every 4 months in the first year of life, and then annually until the age of 4 years. To date, there have been 1564 patients enrolled in the PIANO registry. The survey on vaccine responses was administered to women who had an infant at least 12 months of age between July 2013 and October 2016. Among 211 such women, 179 completed the vaccine survey (85%) and were included in this analysis. In the United States, during the first year of life, the Centers for Disease Control and Prevention recommends hepatitis B vaccines at birth, age 1 to 2 months, and age 6 months; diphtheria–tetanus–pertussis, Pneumococcal, inactivated polio vaccine, and rotavirus at age 2, 4, and 6 months; *Haemophilus influenzae B* (HiB) at 2, 4, and 12 months; and measles, mumps, and rubella at age 12 months. There were 261 infants who were at least 7 months of age during this period; 50 mothers agreed to test for vaccine titers in their infants. Although women could be enrolled during more than 1 pregnancy in PIANO, there were no multiple enrollees in this vaccine substudy.

For this study, women and infant pairs were classified into 2 groups. The biologic-exposed group consisted of those infants in whom the mother had been exposed to any biologic therapy (infliximab, adalimumab, certolizumab pegol, golimumab, natalizumab, vedolizumab, or ustekinumab), either as a single agent or in combination with an immunomodulator at any time between conception and delivery. The no-biologic comparator population consisted of infants whose mothers had been on mesalamine, antibiotics, steroids, immunomodulator monotherapy (azathioprine or 6-mercaptopurine), or received no therapy between conception and delivery.

Vaccination Questionnaire and Titer Measurement

This substudy included all patients with an infant at least 7 months of age at the time of study initiation. Women who consented to participate were mailed a letter to be delivered to their infant's pediatrician requesting measurement of vaccination response. A sample of 2 mL infant blood was obtained to measure response to tetanus toxoid and HiB vaccination after completion of primary immunizations at 2, 4, and 6 months of age. Serologic titers were measured at local laboratories. Vaccination response was considered adequate (within the immune range for that laboratory) or inadequate (below the immune range). These 2 vaccines were selected because they each represent a distinct type of antigen; the tetanus toxoid is a pure protein antigen whereas *HiB* represents a protein–polysaccharide conjugate.[6] Both vaccines

depend on optimal T-helper and B-cell responses. Prior studies have reported that between 90% and 100% of children who completed the primary series achieved protective antitoxin titers against tetanus toxoid[10,11] and HiB.[12–14] Women also were asked specifically if the rotavirus vaccine was administered, and, if not, the reason for skipping the vaccine. Information was obtained about completion of the primary immunization series and reasons for missed vaccines.

Cord blood and/or infant serum was assayed for concentrations of infliximab, adalimumab, certolizumab pegol, vedolizumab, or ustekinumab from a subset of women enrolled in the study. Maternal, cord, and infant serum were collected on the day of birth (0.5–2 mL blood required per sample). If the infant had a detectable concentration of biologic drug at birth, the site coordinators contacted the mother to obtain additional infant samples at months 3 and 6, as appropriate. Maternal and cord blood samples were collected into tiger-top tubes and from the baby into a gold-top tube. The specimens then were packaged by hospital phlebotomy staff or a nurse and shipped ambient to Prometheus Laboratories, Inc (San Diego, CA). Serum concentrations of all drugs were determined at Prometheus Laboratories, Inc, by mobility shift assay as previously described.[15] The assays for infliximab, adalimumab, and vedolizumab have been validated and are in routine clinical use.

Statistical Analysis

All statistical analyses were performed at the Data Management Center at the University of North Carolina at Chapel Hill. Continuous variables were summarized using means and SDs and compared using the *t* test, whereas categoric variables were expressed in proportions and compared using the chi-square test with the Fisher exact modification when appropriate. Rates of adequate vaccination response to tetanus toxoid and HiB were compared across the biologic-exposed and unexposed groups. Univariate logistic regression was performed to quantify the effect of medication exposure on adequate vaccination response, with a 2-sided *P* value less than .05 indicating statistical significance. Analyses were repeated excluding certolizumab pegol users given the known minimal transplacental transfer of this agent. Nonparametric tests were used to compare the median cord levels of infliximab between vaccine responders and nonresponders. The study was approved by the Institutional Review Board at each participating institution.

Results

The study population included 179 women from the PIANO registry who completed the vaccination survey. The mothers' mean age was 31.6 years and the mean disease duration at the time of pregnancy was 9.5 years (Table 1). Two-thirds (67%) had Crohn's disease (n = 120). One third of women each were in their first (n = 67; 37%) or second pregnancy (n = 55; 31%), while 24 women (13.4%) were in their fourth or subsequent pregnancy. Most women had inactive (77%) or mild disease activity (18%) at the time of pregnancy. Eleven women (6%) were on no immunosuppressive therapy, 15 women (8%) were on immunomodulator therapy, and the remaining women were on biologics either as monotherapy (116; 65%) or in combination with an immunomodulator (37; 21%). There was no statistical difference in the mean age, type of IBD, smoking status, gravidity, or disease activity across the 2 groups (Table 1). Vaccine titers were available to infants born to 50 women. Characteristics of mothers with available vaccine titers are shown in Table 2. Among the 42 biologic-exposed patients, 27 were on infliximab, 7 were on adalimumab, 3 were on certolizumab, 2 each were on natalizumab and ustekinumab, and 1 was on vedolizumab. Eight infants born to women on immunomodulators alone or no immunosuppressive therapy formed the comparator population.

Table 3 describes the percentages of women in each subgroup whose infants received the scheduled vaccinations during their first year of life. Most infants in both groups received hepatitis B, diphtheria–tetanus–pertussis, inactivated polio, HiB, pneumococcal, measles-mumps-rubella, and varicella vaccines. Infants born to women on biologic monotherapy or combination therapy (35%) were significantly less likely to have received the rotavirus vaccine compared with those on no immunosuppression ($P = .001$). Among biologic-exposed infants, the rate of receiving the rotavirus vaccine was lower in women on combination therapy (16%) compared with those on biologic monotherapy (41%; $P = .006$). A majority of the women who reported skipping the rotavirus vaccines for their infants did so on their doctors' advice (n = 72), with only 2 and 3 women, respectively, reporting skipping the dose because of personal preference or concern for side effects.

Information on serologic response to the HiB vaccine and to tetanus toxoid was available for 46 and 49 infants, respectively (Figure 1). For the HiB vaccine, 71% of biologic-exposed patients had adequate antibody titers compared with 50% of unexposed infants ($P = .41$) (odds ratio [OR], 2.45; 95% CI, 0.52–11.60). Similarly, for tetanus toxoid, 80% of infants exposed to biologic therapy showed adequate immune responses compared with 75% of unexposed infants ($P = .66$; OR, 1.38; 95% CI, 0.23–8.13). There was no difference in response to the vaccines by type of biologic therapy. The results also were unchanged when excluding certolizumab pegol, which has negligible rates of placental transfer (OR for adequate vaccine response in biologic-exposed compared with unexposed infants was as follows: HiB: 2.25; 95%

Table 1. Characteristics of Included Patients

Characteristics	Biologic exposed (n = 153)	Biologic unexposed (n = 26)
Mean age, *y* (SD)	31.4 (4.6)	33.1 (3.2)
Type of IBD, N (%)		
Crohn's disease	107 (69.9)	13 (50.0)
Ulcerative colitis	43 (28.1)	11 (42.3)
IBDU	3 (2.0)	2 (7.7)
Mean duration of disease, *y* (SD)	8.9 (6.0)	13.2 (7.6)
Smoking status, N (%)		
Never	112 (73.2)	18 (69.2)
Former/current	41 (26.8)	8 (30.8)
Gravidity, N (%)		
1	54 (35.3)	13 (50.0)
2	47 (30.7)	8 (30.8)
3	32 (20.9)	1 (3.8)
≥4	20 (13.1)	4 (15.4)
Disease activity, N (%)		
None	117 (77.0)	19 (79.2)
Mild	26 (17.1)	5 (20.8)
Moderate	8 (5.3)	0 (0.0)
Severe	1 (0.7)	0 (0.0)
Medication use, N (%)		
Biologics	153 (100.0)	0 (0.0)
Immunomodulators	37 (24.2)	15 (57.7)
Mesalamine, steroids, antibiotics, or no therapy	N/A	11 (42.3)

IBDU, IBD unspecified; N/A, not applicable.

CI, 0.45–11.33; tetanus: 1.60; 95% CI, 0.25–10.36). Among the 42 women on biologic therapy, 10 were on combination therapy with an immunomodulator. There was no difference in the proportion with adequate serologic response to either HiB (69% vs 78%) or tetanus (84% vs 67%) between the biologic monotherapy and combination therapy groups, respectively.

Table 2. Characteristics of Women With Available Infant Vaccine Titers

Characteristics	Biologic exposed (n = 42)	Biologic unexposed (n = 8)
Mean age, *y* (SD)	31.7 (3.4)	30.6 (4.4)
Mean disease duration, *y* (SD)	10.4 (5.6)	5.3 (2.3)
Type of IBD (%)		
Crohn's disease	30 (71.4)	4 (50.0)
Ulcerative colitis	11 (26.2)	4 (50.0)
IBDU	1 (2.4)	0 (0.0)
Ever smoker (%)	5 (11.9)	2 (25.0)
Disease activity (%)		
None	34 (81.0)	5 (62.5)
Mild	8 (19.0)	3 (37.5)
Medication use, N (%)		
Biologics	42 (100.0)	0 (0.0)
Immunomodulators	10 (23.8)	2 (25.0)
Mesalamine, steroids, antibiotics, or no therapy	N/A	6 (75.0)

IBDU, IBD unspecified; N/A, not applicable.

Table 3. Proportion of Infants Receiving at Least 1 Dose of Each of the Vaccines

Characteristics	Biologic unexposed (n = 26), %	Biologic exposed (n = 153), %	*P* value
Hepatitis B	81	75	.51
DTAP	85	83	.80
IPV	85	82	.71
HiB	85	83	.80
Pneumococcal	85	83	.80
MMR	81	82	.90
Rotavirus	69	35	.001[a]
Varicella	81	83	.80

DTAP, diphtheria, tetanus, pertussis; IPV, inactivated polio vaccine; MMR, measles, mumps, rubella.
[a]In the United States, during the first year of life, the Centers for Disease Control and Prevention recommend hepatitis B vaccines at birth, 1 to 2 months, and 6 months; diphtheria-tetanus-pertussis, pneumococcal, and inactivated polio vaccine at 2, 4, and 6 months; HiB at 2, 4, and 12 months; MMR at 12 months; and rotavirus at 2, 4, and 6 months.

Both groups had response rates similar to infants born to mothers on no immunosuppression.

Serum drug concentrations were available for 29 infants (20 infliximab, 6 adalimumab, and 1 each for certolizumab, ustekinumab, and vedolizumab) and 33 cord blood samples (23 infliximab, 6 adalimumab, 2 ustekinumab, and 1 each for vedolizumab and certolizumab). For tetanus toxoid, there was no difference between the rates of response in infants with undetectable (50%), therapeutic (3–10 mcg/mL; 100%), high (10.1–20 mcg/mL; 83%), and very high (>20 mcg/mL) biologic concentrations ($P = .37$). Similarly, there was no association between response to HiB across the same 4 categories (50%, 83%, 100%, and 59%, respectively; $P = .22$). Because infliximab was the most commonly used biologic, we performed a subgroup analysis of women on this therapy. There was no association between infliximab concentration in cord blood and adequacy of immune response to HiB or tetanus vaccines (Figure 2). The median cord blood infliximab concentrations were similar between infants with an adequate (24.3 mcg/mL; interquartile range, 14.0–42.7 mcg/mL) or inadequate immune response to HiB (43.0 mcg/mL; interquartile range, 28.5–53.3) ($P = .31$). Similarly, for tetanus toxoid, there was no difference in the median infant cord level between those with (31.4 mcg/mL) and without (41.5 mcg/mL) an adequate immune response ($P = .93$).

Infants born to 43 of the women on biologics (19 infliximab, 12 certolizumab, 7 adalimumab, 1 infliximab and certolizumab, and 1 ustekinumab) received the rotavirus vaccines. Among infants of 40 women for whom these data were available, 7 (17.5%) reported a reaction to the vaccine. Of these, 6 infants had a fever (5 infliximab, 1 adalimumab) and 1 had diarrhea (on infliximab). There was no correlation between infant drug concentration at birth and the likelihood of a reaction to the rotavirus vaccine (Table 4).

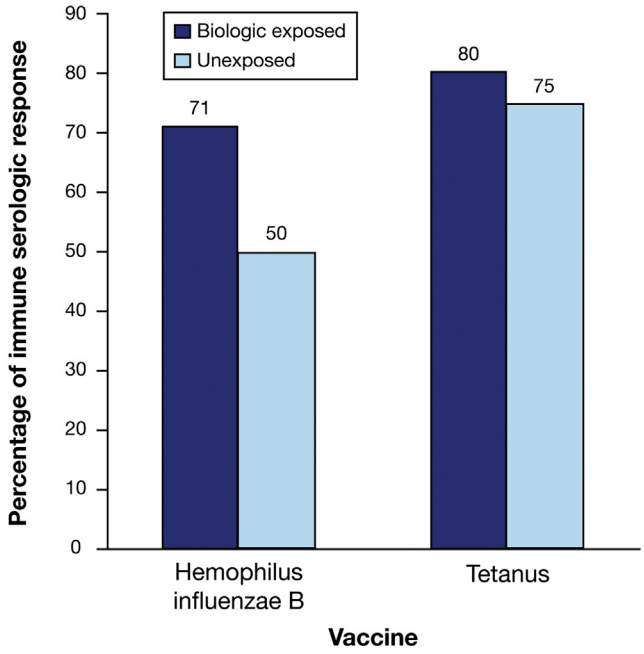

Figure 1. Proportion of infants with protective titers to HiB and tetanus vaccine, by maternal biologic use. A total of 46 (38 biologic exposed, 8 unexposed) and 49 (41 biologic exposed, 8 unexposed) infants had an available vaccine titer response to HiB and tetanus, respectively.

Discussion

The impact of medications used for the management of maternal IBD on the health and development of infants historically has not been studied systematically. With data showing that in utero exposure to some biologics leads to persistence of drug concentrations for up to a year, there is a need for robust examination of this effect on infant immune response. By using data from a rigorously followed up prospective cohort of pregnant women with IBD, we show that the rates of adequate serologic response to HiB and tetanus vaccines were similar among infants born to women on biologic therapy compared with those who were not biologic users during pregnancy. There was also no association between cord blood or infant serum concentrations of biologics and adequacy of vaccine titers. In a small subset of infants exposed to maternal biologic therapy, rotavirus vaccine was administered without serious adverse reactions and with mild events occurring at a rate similar to that expected in the general population, suggesting a need for further studies in this population.

There is a significant body of literature examining the effect of immunosuppression on response to vaccination in patients with IBD, primarily in response to the influenza vaccine.[9] Mamula et al[9] studied 80 children (51 with IBD) who received a single dose of the inactivated influenza vaccine. Compared with healthy controls, nearly all of whom (89%–100%) developed protective titers to 3 different influenza virus antigens, only 33% to 85% of patients with IBD showed protection for all 3 antigens. The reduced serologic response was more striking in patients on combination therapy. Some studies identified similar rates of initial response, but reduced persistence of the seroprotective titers at 2 years.[16] In adult IBD patients, Melmed et al[3] showed that those on combination anti-TNF immunomodulator therapy had lower rates of response to the pneumococcal polysaccharide vaccine (45% vs 80% with no immunosuppression). Dezfoli et al[17] showed lower rates of response to the tetanus vaccine in patients on combination therapy with anti-TNF and immunomodulator compared with those on no immunosuppression.

Examination of the adequacy of vaccine response in infants born to women on biologic therapy attained additional impetus, with emergence of data suggesting persistence of detectable biologic concentrations in infants for many months after delivery. A prospective observational cohort by Julsgaard et al[4] showed that infliximab concentration could persist for up to 12 months and adalimumab for 9 months after birth. In contrast, certolizumab pegol, by virtue of being a

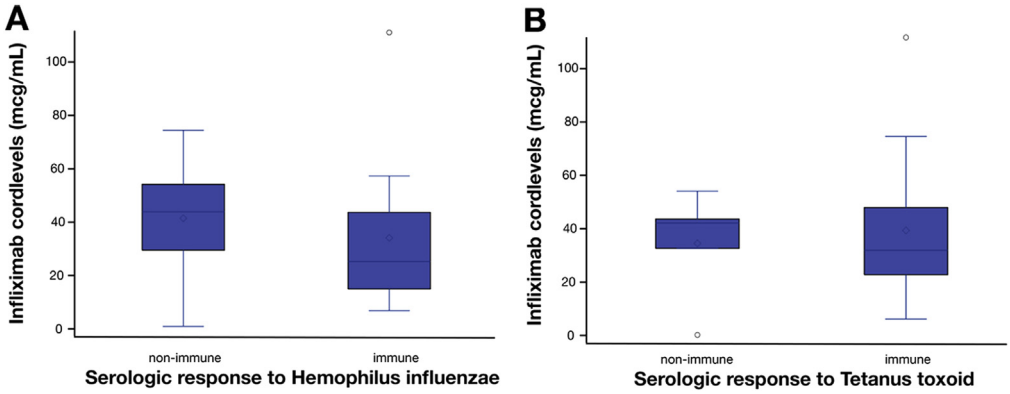

Figure 2. Association between the cord blood concentration of infliximab and the response to HiB or tetanus toxoid vaccines. (*A*) HiB. The median infliximab cord blood levels in infants with adequate and inadequate serologic response to HiB were 24.3 and 43.0 mcg/mL, respectively ($P = .30$). (*B*) Tetanus toxoid. The median infliximab cord blood levels in infants with adequate and inadequate serologic response to tetanus were 31.4 and 41.5 mcg/mL, respectively ($P = .93$).

Table 4. Characteristics of Infants Born to Mothers on Biologic Therapy Who Received the Rotavirus Vaccine

Biologic therapy	Number	Proportion with reaction, N (%)	Type of reaction	Biologic level in infant, *mcg/mL*
Infliximab	19	6 (32)	Fever (n = 5) Diarrhea (n = 1)	Diarrhea: 72 mcg/mL (at birth; 5 mcg/mL (at 3 mo) No reactions: 44, 11, 42, 28, 22, and 69 mcg/mL
Adalimumab	7	1 (14)	Fever (n = 1)	No reaction: 14, 7 mcg/mL
Certolizumab	12	0 (0)	-	No reaction: 5 mcg/mL
Ustekinumab	1	0	None	No reaction: 40 mcg/mL

polyethylene glycolylated FaB immunoglobulin, does not bind to the neonatal Fcγ receptor responsible for transplacental transfer and was not found in infant or cord blood.[18] In this context, it is reassuring to note that in our study, infants exposed to maternal biologic (or immunomodulator therapy) had similar rates of serologic response to HiB or tetanus vaccines compared with infants of unexposed women in our cohort. However, the overall rates of adequate response to HiB and tetanus in our cohort, 67% and 80%, respectively, were lower than noted historically. Prior studies reported that between 90% and 100% of children who completed the primary series achieved protective antitoxin titers against tetanus toxoid[10,11] or HiB.[12,13] Two reasons could explain the lower rates of response observed in our cohort: a possible immunosuppressive effect of maternal IBD itself or the impact of in utero exposure to maternal immunosuppressive and biologic use, which our small sample size prevents us from distinguishing.

Despite the recommendations to avoid live vaccines in infants born to mothers on biologic therapy, infants born to 43 women on biologics received the rotavirus vaccine with just fewer than 1 in 5 developing a minor reaction. This is comparable with the rates of fever (42%) or diarrhea (19%) reported in the healthy infants in the general population in the Vesikari et al[19] publication that included more than 34,000 infants. In addition, it has been reported that the first dose of rotavirus vaccine given after 3 months of age in healthy infants was associated with an increased risk of intussusception.[20,21] Prior studies of infants with severe immunodeficiency have shown severe live vaccine associated reactions[22] and Cheent et al[5] described a case of severe, disseminated Bacillus–Calmette–Guerin infection resulting in death after vaccination at 3 months in an infant exposed to maternal infliximab. In a systematic review, Croce et al[23] described the safety of live vaccines in 21,082 patients on immunosuppressive therapy for immune-mediated disease (majority of study sample) or organ transplantation, most of whom received the herpes zoster vaccine. Local or systemic reactions were infrequent, occurring in 1.3% of the cohort. However, none of the reports described patients receiving the rotavirus vaccine. Despite our data suggesting a lack of severe side effects with the rotavirus vaccine in these infants, in the absence of robust evidence, one should continue to avoid live vaccines in infants born to mothers on biologic therapy (excluding certolizumab) during the first year of life or until drug clearance is confirmed. With the growing availability of tests, one conceivably could test serum drug concentration in infants, and, if undetectable, consider live vaccination at that time, if appropriate for the vaccine, particularly in infants most likely to benefit from such vaccines.

We acknowledge several limitations to our study. Although this was a large study of vaccination response in infants of mothers on immunosuppressive and biologic medications, the number of children, particularly on no immunosuppression, was small and thus provided limited statistical power. However, of note, a few prior studies on vaccine responses in individuals with IBD had only modestly larger sample sizes (60–64 patients) and showed a statistically significant reduction in serologic response in immunosuppressed individuals. In addition, inclusion in this study relied on the willingness of mothers to subject their healthy, unaffected infants to invasive blood draws at older than 7 months of age, which was an understandable practical constraint, limiting sample size. We assessed the serologic response to only 2 vaccines, chosen because they provide a window into immune responses to protein and protein–polysaccharide vaccines. Drug levels were analyzed at a single time point (birth) given the smaller number of patients with levels available at 3 and 6 months. Because the vaccines are administered at multiple time points, measurement of infant infliximab levels at each of these doses would be impractical. There is a need for future studies to examine the sustainability of response to vaccination in such infants.

In conclusion, despite the growing body of literature showing that both conventional immunomodulator therapy with thiopurines (6-mercaptopurine, azathioprine), TNFα antagonists, anti-integrin, or anti-interleukin 12/23 therapies are low risk during pregnancy and are not associated with congenital anomalies and pregnancy outcomes, the short- and long-term impacts on immune response in the infant has yet to be determined. This study was a large prospective study that looked at infants exposed to maternal immunomodulator or biologic use and infant vaccine response. In our infants, maternal immunosuppression use was not associated with lower rates of response to tetanus or HiB vaccines compared with unexposed infants of mothers with IBD, however, overall rates of response were lower than historically reported. In a limited cohort of exposed

infants given the rotavirus vaccine, there was no association with significant adverse reactions.

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Conflicts of interest
These authors disclose the following: Ashwin Ananthakrishnan has served on scientific advisory boards for Abbvie, Takeda, and Merck; Dawn Beaulieu has served as a consultant for Abbvie; Russell Cohen has served on the speaker's Bureau for Abbvie and Takeda, has served as a consultant/on the advisory board/on the scientific advisory board for Abbvie, Celgene, Entera Health, Hospira, Janssen (Johnson & Johnson), Pfizer, Sandoz Biopharmaceuticals, Takeda, and UCB Pharma, has been the principal investigator for clinical trials for Astra-Zeneca, Celgene, Gilead Sciences, Medimmune, Mesoblast Ltd, Osiris Therapeutics, Pfizer, Receptos, RedHill Biopharma, Sanofi-Aventis, and UCB Pharma; Sunanda Kane has served as a consultant for Abbvie, Janssen, Samsung Bioepis, 11 Health, and Spherix Global Health, has received research funding from UCB, and has served on the GI Specialty Board for ABIM; and Uma Mahadevan has served as a consultant for Abbvie, Janssen, UCB, and Takeda. The remaining author discloses no conflicts.

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