



# Plant-based diet for pregnant women with inflammatory bowel disease: case series

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**Background:** We assert that the ubiquitous environmental factor in inflammatory bowel disease (IBD) is our westernized diet. Therefore, all of our newly diagnosed patients were admitted to experience a plant-based diet (PBD). In the present study, we investigated the efficacy of a PBD in pregnant women with IBD.

**Case Description:** Included in the study were women with IBD provided with a PBD (lacto-ovo-vegetarian diet) between 2004 and 2020 who were either pregnant or became pregnant. There were 10 pregnancies in eight cases: seven cases of ulcerative colitis (UC) and one case of Crohn's disease (CD). Five active cases during pregnancy were treated. The other five cases experienced the diet before pregnancy. Two cases developed UC either during pregnancy or in the postpartum period. The PBD without medication induced remission in two mild cases of UC. Infliximab and the PBD induced remission in a relapsed case of CD. There were six conceptions during remission without medication in four cases of UC. No case relapsed during pregnancy in these cases. Vaginal, cesarean, and vacuum extraction were undertaken in four, four, and two deliveries, respectively. Three in two cases were preterm deliveries. There were 10 live births in the eight cases. Two neonates from a mother had jaundice. In the median follow-up period of 71 months, all eight cases were in the quiescent phase. PBD scores in their follow-up period, which indicate adherence to the PBD, exceeded the baseline scores.

**Conclusions:** Our case series study indicated that a PBD was effective for pregnant women with IBD.

**Keywords:** Infliximab; plant-based diet (PBD); pregnancy; inflammatory bowel disease (IBD); case series

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## Introduction

Inflammatory bowel disease (IBD) was initially a disease seen primarily in western countries, but it became a global one since around the turning of the 21st century (1,2). It occurs in genetically susceptible individuals due to an environmental factor(s). But there has not been a widely appreciated ubiquitous environmental factor. Our

prior research has suggested a strong association between a westernized diet and IBD (3). A westernized diet is characterized by increased consumption of animal fat, animal protein, and sugar with decreased consumption of carbohydrates (3). Therefore, we advise all newly diagnosed patients to be admitted and to experience a plant-based diet (PBD) (lacto-ovo-vegetarian diet) to counter omnivorous

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western diets (4). Outcomes of our modality incorporating PBD surpassed current standards in both ulcerative colitis (UC) and Crohn's disease (CD) in both the induction and quiescent phases (4-9). Based on our outcomes together with recent findings in epidemiology, nutrition, microbiology, immunology, and multi-omics studies, we were the first to recommend PBD for IBD in the literature (6-9).

Because the peak incidence of IBD coincides with the reproductive years, specific attention has been paid to pregnancy. Pregnancy *per se* does not increase the relapse rate in IBD. In UC, the relapse rate per year in patients with and without pregnancy was 34% and 32%, respectively (10). Pregnancy-related adverse events (still birth, preterm birth, small for gestational age, low birth weight, congenital abnormalities, cesarean section) are found more often in pregnancy with IBD than in pregnancy without IBD (11).

### Highlight box

#### Key findings

- Plant-based diet (PBD), a lacto-ovo-vegetarian diet, was provided in eight cases of inflammatory bowel disease (IBD) during or before pregnancy. PBD induced remission in mild cases of ulcerative colitis (UC) without medication. Infliximab and PBD as first-line therapy induced remission in a case of Crohn's disease (CD). There were six conceptions during remission in four cases of UC. No patients relapsed during pregnancy in these cases. There were 10 live births in the eight cases. In the median follow-up period of 71 months, all eight cases were in the quiescent phase, and five of them were without medication.

#### What is known and what is new?

- The authors assert that IBD is a lifestyle disease mainly mediated by a westernized diet, and we developed PBD to counter a westernized diet. Outcomes of our modality incorporating PBD surpassed current standards in both UC and CD in both the induction and quiescent phases. Based on our clinical outcomes together with interdisciplinary data, we now recommend PBD for IBD. PBDs are known to be associated with reduced risk of gestational hypertension and diabetes.
- This is the first study focusing on the effect of PBD in pregnant women with IBD. The results indicated that PBD was effective for pregnant women with IBD.

#### What is the implication, and what should change now?

- Current westernized diets induced diet-related common chronic diseases. IBD is not an exception. Relapse of CD cannot be prevented by balanced meals of westernized diets, but it can be prevented by PBDs. Current global diets are problematic and pro-inflammatory, while PBDs are healthy and anti-inflammatory. Appreciation of the critical role of diet and widespread adoption of PBDs are needed in IBD.

Activity of IBD increases the risk of maternal and fetal complications such as spontaneous abortion, prematurity, developmental defects, and still birth (12). Because conception in the active phase of IBD causes a significantly higher risk of adverse events of pregnancy than that in remission (13), conception in the quiescent phase is recommended (14,15).

As for diet, a well-balanced, healthy diet is described (15). Even balanced meals could not prevent relapse of CD (4,7-9). To our knowledge, there are no other reports in the literature of pregnant women with IBD treated with a modality incorporating PBD. Therefore, this is the first report focusing on the effect of PBD in pregnant women with IBD. We present this article in accordance with the AME Case Series reporting checklist (available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-67/rc>).

### Case presentation

Protocol of this study was approved by the Ethical Committee of Nakadori General Hospital and by the Ethical Committee of Akita City Hospital (Protocol number: 19-2003, 12-2013, 15-2015). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for the publication of this case series and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Cases were prospectively studied. There were eight consecutive pregnant cases with IBD (UC =7 and CD =1) provided with PBD between 2004 and 2020 in Akita City Hospital and Nakadori General Hospital. There were 10 pregnancies in these cases. Patients with mild UC or UC in remission who did not need immediate treatment were advised to be admitted at a convenient time, e.g., seasonal holidays. We call this educational hospitalization (9). All inpatients including conventional hospitalization, were provided with educational material on lifestyle diseases, pathogenesis of IBD, healthy lifestyle habits (16), and PBD. At the end of the hospitalization, a qualified dietitian gave dietary guidance to the patient. Patients were advised to continue with the PBD after discharge. Patients were followed up as long as possible.

PBD was a lacto-ovo-vegetarian diet that allowed consumption of fish once a week and meat every other

**Table 1** Active IBD during pregnancy: treatment by modality incorporating PBD followed by delivery

Case	Age (years)	IBD			Obstetric history	Hospitalization				Delivery			Feeding	
		IBD	Type (18)	Disease duration		Gestation	Reason of hospitalization	Days	IBD		Mode	Mother		New-born
									Treatment	Outcome				
1	28	UC	Initial case E1: proctitis S1: mild	1 m	G 1 P 0	8 w 4 d	EH	6	No medication	Remission	Vaginal at 41 w 3 d	Sound	Sound	Breast
2	36	UC	Initial case E1: proctitis S1: mild	1 m	G 1 P 0	22 w 35 w 5 d	EH (PO-UC) threatened Abortion TPTL	10 7	No medication	Remission	Vaginal at 40 w 0 d	Sound	Sound	Breast
3	29	UC	Relapse case E2: left sided S3: severe	6 y 5 m	G 0 P 0	12 w	Relapse (severe)	58	TPN, PS (i.v.), G-CAP mesalamine	Remission	CS: fetal distress at 39 w 0 d	Sound	Sound	Breast
	30				G 1 P 1	Post-partum 2 w 4 d	Relapse (severe)	57	TPN, PS (i.v.), G-CAP, AZA mesalamine	Remission				
4 <sup>†</sup>	26	CD	Relapse case L3: ileocolonic B2: stricturing	3 y 8 m	G 0 P 0	26 w 0 d 29 w 5 d	Relapse & TPTL	20 3	1st IFX infusion 2nd IFX infusion	Remission	CS: CPD at 39 w 2 d	Sound	Sound	Breast
5 <sup>†</sup>	29	UC	Initial case E2: left sided S2: moderate	1.5 m	G 1 P 1	Post-partum 27 w	EH (PO-UC)	12	Mesalamine	Reduction of dosage from 3.2 to 0.5 g/d		n.a.		Breast

<sup>†</sup>, the same cases 4 and 5 in *Table 2*, respectively. y, year(s); m, month(s); w, week(s); d, day(s); IBD, inflammatory bowel disease; PBD, plant-based diet; UC, ulcerative colitis; CD, Crohn's disease; G, gravidity; P, parity; EH, educational hospitalization; PO-UC, pregnancy-onset UC; TPTL, threatened preterm labor; TPN, total parenteral nutrition; PS (i.v.), intravenous infusion of prednisolone 60 mg/d; G-CAP, granulocyte apheresis (19); AZA, azathioprine; IFX, infliximab; CS; caesarean section; CPD, cephalopelvic disproportion; n.a., not applicable.

week (4). The details of PBD were previously described (4). Using a food-frequency questionnaire, we developed a simple way to evaluate adherence to the PBD for Japanese patients with IBD (17). A higher PBD score (PBDS) indicates a greater adherence to PBD. The score of PBD during hospitalization was 35. The PBDS was evaluated on admission (baseline PBDS) and again within and beyond 2 years after discharge, referred to as short-term and long-term PBDS, respectively (5,9).

*Table 1* shows five active cases during pregnancy, and *Table 2* shows the other five cases who experienced the diet before pregnancy, and then conceived after an interval from 9 months to 8 years. Two cases were duplicates. Both tables show the demographics of cases including ages,

phenotypes and severity of IBD (18), treatment (19) and outcome of IBD, and outcomes of pregnancy. Five of the eight cases (Cases 3, 4, and 6–8) were included in previous interventional studies without reproductive matters (7,9). Two cases (Cases 2 and 5) developed UC during pregnancy and in the postpartum period, respectively, namely pregnancy-onset UC (PO-UC) (20). These two cases were separately reported as case reports (21,22).

In this case series, there were five cases of educational hospitalization (*Tables 1,2*). Apart from patients already on medication prescribed by their previous doctor (Cases 5–7), PBD was provided without medication during an educational hospitalization in Cases 1 and 2. The PBD without medication induced remission in these two mild

**Table 2** Treatment of active IBD by modality incorporating PBD and pregnancy thereafter

Case	Age (years)	IBD						Period until gestation	IBD at the time of conception		Relapse of IBD during pregnancy	Delivery			Feeding
		IBD Type (18)	Disease duration	Hospitalization			Phase (18)		Medication	Mode		Mother	New-born		
				Medication	Days	Outcome									
6	34	UC	Relapse case E3: pancolitis S1: mild	6 y	Mesalamine (oral & enema)	EH 6	Remission	8 y	S0	None	No	Vaginal at 40 w	Sound	Sound	Breast
7	27	UC	Relapse case E1: proctitis S1: mild	11 m	Mesalamine (oral & local)	EH 10	Unchanged	4 y	S0	None	No	Vacuum extraction: weak labor at 37 w 4 d	Sound	Jaundice	Breast
								6 y	S0	None	No	Vacuum extraction: NRFS at 36 w 2 d	Sound	Jaundice	Breast
8	28	UC	Initial case E3: pancolitis S2: moderate	4 m	PS (oral) Mesalamine (oral)	24	Remission	5 y	S0	None	No	CS: fetal distress at 35 w 5 d	Sound	Sound	Breast
			7 y					S0	None	No	CS at 36 w 6 d	Sound	Sound	Breast	
4 <sup>†</sup>	26	CD	Initial case L3: ileocolonic B2: stricturing	3 y 2 m	IPF therapy Mesalamine	49	Remission	9 m	Remission	Mesalamine	Yes	See Table 1			
5 <sup>†</sup>	31	UC	Initial case E2: left sided S2: moderate	1.5 m	Mesalamine	EH 12	Reduction of dosage from 3.2 to 0.5 g/d	10 m	S0	None	No	Vaginal at 40 w 3 d	Sound	Sound	Breast

See Table 1

<sup>†</sup>, the same cases 4 and 5 in Table 1, respectively. y, year(s); m, month(s); w, week(s); d, day(s); IBD, inflammatory bowel disease; PBD, plant-based diet; UC, ulcerative colitis; CD, Crohn's disease; PS, prednisolone; IPF therapy, infliximab and PBD as first-line therapy; EH, educational hospitalization for IBD; S0, remission; NRFS, non-reassuring fetal status; CS, caesarean section.

cases. In this case series, remission was defined as the disappearance of active symptoms in both diseases (7,9). Infliximab and the PBD induced remission in a relapse case of CD (Case 4) (Table 1). There were six conceptions during remission without medication in four cases of UC. No cases relapsed during pregnancy in these cases (Table 2). Vaginal, cesarean, and vacuum extraction delivery were performed in four, four, and two deliveries, respectively. Three pregnancies in two cases were preterm delivery (Table 2). There were 10 live births in the eight cases. Two new-born babies from a mother (Case 7) had neonatal jaundice (Table 2).

In the median follow-up period of 71 months after

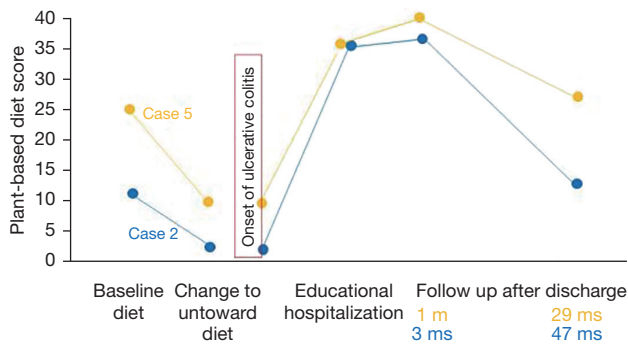
the 1st hospitalization experiencing PBD, all eight cases were in the quiescent phase (Table 3). Five cases were free of medication. One case was on mesalamine. One case was on betamethasone suppository as needed. One patient with CD received scheduled infliximab infusion. The mean short-term PBDS [standard deviation (SD)] was 28.4 (9.4) at a median follow-up period of 6 months, which was higher than the 12.0 (7.7) at baseline ( $P=0.0061$  by paired  $t$ -test). The mean long-term PBDS (SD) was 21.4 (6.8) at a median follow-up period of 47 months, which was higher than the 14.4 (10.9) at baseline ( $P=0.10$ ) (Table 3).

Additional notes of cases were in the followings.

**Table 3** Follow-up of pregnant women with IBD treated by modality incorporating PBD and follow-up of their PBDS

Follow-up & PBDS	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Mean [SD]	Median [IQR]
Final follow-up										
Period after 1st hospitalization (months)	12	65	51	87	47	223	76	161	90 [69]	71 [48–143]
Stage (severity)	S0	S0	S0	Remission	S0	S0	S0	S0	–	–
Medication	None	None	None	Scheduled IFX maintenance	None	Mesalamine	Betamethasone supp as needed	None	–	–
PBDS										
Base	8	11→2 <sup>†</sup>	11	5	25→9 <sup>†</sup>	27	22	4	14.1 [9.2]	11.0 [5.8–24.3]
Short term										
PBDS	19	36	20	27	40	Not available	Not available	Not available	28.4 [9.4]	27.0 [19.5–38.0]
Follow-up period (months)	12	3	6	6	1	Not available	Not available	Not available	5.6 [4.2]	6 [2–9]
Long term										
PBDS	Not applicable	12	Not applicable	20	27	29	Not applicable	19	21.4 [6.8]	20.0 [15.5–28.0]
Follow-up period (months)	Not applicable	47	Not applicable	40	29	120	Not applicable	85	64 [38]	47 [35–103]

<sup>†</sup>, changed diet prior to onset of ulcerative colitis. Not available: not available was due to the author’s failure to obtain a food-frequency questionnaire during follow-up. IBD, inflammatory bowel disease; PBD, plant-based diet; PBDS, plant-based diet score; SD, standard deviation; IQR, interquartile range; S0, remission in severity of ulcerative colitis (18); IFX, infliximab; supp, suppository.



**Figure 1** Change in plant-based diet scores over time in PO-UC patients (Case 2 and Case 5). m, month; ms, months; PO-UC, pregnancy-onset ulcerative colitis.

**Case 1**

Four days after being admitted for educational hospitalization, blood on defecation was not observed. The result of a fecal immunochemical test (FIT) (reference <100 ng/mL) on discharge was <50 ng/mL. The time course

indicated that the conception preceded the symptom of proctitis (bloody stool).

**Case 2**

This was a case of PO-UC and was reported (21). The follow-up study beyond the case report showed that her short- and long-term PBDSs were 36 and 12, respectively (Table 3, Figure 1).

**Case 3**

In 2008, she affected with severe UC was referred to us. Total parenteral nutrition was undertaken. Intravenous prednisolone 60 mg/day, the standard first choice for severe colitis (19), was ineffective. Granulocyte apheresis twice a week (19) was added, resulting in improvement. PBD (800 kcal/day) was then initiated and gradually increased to 1,700 kcal/day. She was weaned off prednisolone in the outpatient department. She had a cesarean section due to

fetal distress. Severe colitis recurred soon after the delivery. The same strategy as the one taken during pregnancy induced remission. Azathioprine was added this time. Maintenance of remission for 3 years allowed withdrawal of medication (azathioprine and mesalamine). Remission was maintained without medication for 1 year. She was lost to follow-up after deciding to stop visits.

#### Case 4

Infliximab and PBD as first-line (IPF) therapy (7,9) induced remission in CD (Table 2). She took 2.0 g/d of mesalamine. Nine months later she became pregnant in the quiescent phase (Table 1). She was admitted to the obstetric ward at gestation (G) 26 w due to threatened preterm labor and relapse of CD. Infliximab (5 mg/kg body weight) was infused at G 27 w and 29 w, which induced remission. Mother and new-born were sound (Table 1). Cord blood infliximab concentration was 6.21 µg/mL. At aged 179th day, infliximab concentration was 0.01 µg/mL, which was below the active biologic concentration (>0.5 µg/mL). The baby then received BCG vaccine. At 6 weeks postpartum, she relapsed. Therefore, scheduled infliximab maintenance therapy was initiated. The maintenance therapy on an inpatient basis was continued up to the final visit: 52 infusions of infliximab over a 74 months period (Table 3). She had four PBD meals during the 2 days of hospitalization for each infusion. In the meantime, the stricture of the terminal ileum was surgically removed.

#### Case 5

This was a case of PO-UC and was reported (22). The follow-up study beyond the case report showed that her short- and long-term PBDSs were 40 and 27, respectively (Table 3, Figure 1). She had a second baby 19 months after the educational hospitalization. She took mesalamine for mild relapse at 37 months after the educational hospitalization. At the final visit, she was G 11 w and UC was quiescent without medication.

#### Case 6

Onset of UC was at the age of 28 in 1998. She was hospitalized twice (in 1999 and 2003) for relapses before visiting us in 2004. She underwent educational hospitalization. Positive fecal occult blood became negative during the hospitalization: FIT from 533 to 95 ng/mL (Table 2). Eight years later, she became pregnant in S0 (quiescent phase) (18) without medication and

delivered the baby in 2012.

#### Case 7

Faint blood attached to stool was unchanged during educational hospitalization. Therefore, betamethasone sodium phosphate suppository was added. Her symptom subsequently disappeared, resulting in withdrawal of mesalamine. She then used betamethasone suppository as needed. She became pregnant twice (4 and 6 years later).

#### Case 8

UC was diagnosed by her previous gastroenterologist in 2009, after which she was referred to us. Remission was achieved during hospitalization. She was weaned off prednisolone (20 mg/day) (Table 2).

## Discussion

We herein reported eight cases of pregnant women with IBD who were provided with PBD. As expected from our previous series of IBD patients provided with PBD (4-7,9), the outcomes of PBD in pregnant women seemed favorable in general. PBD without medication induced remission in two mild cases of UC. IPF therapy induced remission in a relapsed case of CD. There were six conceptions during remission without medication in four cases of UC. No patients relapsed during pregnancy in these cases. There were 10 live births in the eight cases. In the median follow-up period of 71 months, all eight cases were in the quiescent phase, and five of them were without medication. PBDS during the follow-up period exceeded baseline PBDS.

PBDs are recommended to the public, including pregnant women, as a healthy diet to prevent common chronic diseases such as metabolic syndrome, diabetes mellitus, coronary heart disease, and stroke (23). In addition, PBDs are more environmentally sustainable than meat-based diets and correspond to UN Sustainable Development Goals (23). PBDs are known to be associated with reduced risk of gestational hypertension and gestational diabetes mellitus (24).

There are recent reports focusing on cases in which IBD occurred during pregnancy or postpartum. It was referred to as PO-IBD (20). Unfavorable long-term outcomes were shown to be a feature of PO-UC: lower frequency of long-term remission and more hospitalizations than non-PO-UC (20,25). No concern was shown for dietary factors on relapse



or onset of IBD during pregnancy and postpartum (26). Focusing on diet, we reported onset or relapse of UC during a change in dietary habits toward unhealthy diets: during a low-carbohydrate weight-loss diet and during a busy life, respectively (7,9). Our two cases of PO-UC were typical illustrative cases. The patients were aware that they changed their diets towards unhealthy ones due to emesis or a feeling of being freed from pregnancy and childbirth (21,22). We just pointed out their risky dietary changes, and then they recognized the importance of diet. This seemed to result in them paying greater attention to their diet and its contribution toward relapse prevention (*Figure 1*). Case 2 had been in remission for more than 5 years, and Case 5 had her 2nd child and was going to have a 3rd child. We do not feel that the clinical course of PO-UC is poor compared to non-PO-UC. Onset and relapse of IBD occur more frequently in the first and second trimesters than the third trimester (14,20). The reason for this is not known. Morning sickness is quite common in the first trimester, and it often extends to the second trimester. An investigation on whether dietary change toward an unhealthy one due to morning sickness is related to onset and relapse of IBD is eagerly awaited.

Although Case 4 with CD became pregnant in the quiescent phase, she relapsed during pregnancy and the postpartum. Because infliximab was effective for initial induction, it was natural to use infliximab again for the relapse. Infliximab was used in the late of 2nd trimester (G 26 w) and in the beginning of the 3rd trimester (G 29 w). It has been reported that infliximab and adalimumab cross the placenta, and that their use beyond the second trimester results in neonatal levels of biologics exceeding maternal levels (27). Therefore, we did not provide a third infusion of infliximab based on European Crohn-Colitis Organisation (ECCO) Guidelines (14). The relapse rate in the postpartum in CD according to a recent cohort study was 30% (28). All risk factors for relapse in the postpartum in CD, i.e., stricture type, relapse during pregnancy, and nonuse of infliximab after delivery, applied to her (26). It is of note that the patient in Case 4, who had poor prognostic factors (young onset, late start of treatment due to delayed diagnosis, stricture type), became a mother and was in clinical remission for more than 6 years with infliximab maintenance therapy alone without immunosuppressants or steroids. There is a rapidly growing body of data on maternal and neonatal outcomes by biologic use. Neonatal short- and long-term outcomes have been shown to be the same between biologic use and its non-

use (29). Maintaining quiescence via biologics is preferable to relapse due to withdrawal of biologics for maternal and neonatal outcomes. It is now recommended that biologics be used continuously preconception, throughout pregnancy, and postpartum (15,29,30). Live vaccinations of newborns whose mothers are on anti-tumor necrotizing factor (TNF) antibodies are recommended beyond the first 6 months of life (15,27).

Case 3 was a case of severe UC in 2008 when infliximab was not yet approved for UC in Japan. Because prednisolone (intravenous 60 mg/day), the first-line therapy in current guidelines (20), has several disadvantages (5,31), we replaced prednisolone (glucocorticoid) with infliximab in 2010. IPF therapy induced a high remission rate in severe UC (76%) and a low colectomy rate (6%) (5). We now perform IPF therapy for severe cases of UC like Case 3. Although both severe UC and glucocorticoid therapy increase the risk of preterm birth and low birth weight (32,33), Case 3 delivered a healthy new-born at G 39 w 0 d. Relapse is known to decrease in the years following pregnancy in both UC and CD (34). She was well without relapse during 4 years of follow-up.

It is obvious that our small case series without a control diet does not constitute evidence for the superiority of PBD for pregnant patients with IBD over the current westernized diet. This case series, however, certainly implies the efficacy of PBD for pregnant patients with IBD. We hope that large, controlled studies will validate our findings.

## Conclusions

In conclusion, contemporary guidelines are available for safe pregnancy and a favorable outcome in women with IBD. Conception in the quiescent phase is desirable. Medication(s) including anti-TNF antibodies, used in the quiescent phase should be continued during pregnancy, with the exception of methotrexate. Appreciation of PBD for a healthy diet will further contribute to favorable maternal and neonatal outcomes.

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## Footnote

*Reporting Checklist:* The authors have completed the AME Case Series reporting checklist. Available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-67/rc>

*Peer Review File:* Available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-67/prf>

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://tgh.amegroups.com/article/view/10.21037/tgh-23-67/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Protocol of this study was approved by the Ethical Committee of Nakadori General Hospital and by the Ethical Committee of Akita City Hospital (Protocol number: 19-2003, 12-2013, 15-2015). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for the publication of this case series and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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