Inflammatory Bowel Disease in Pregnancy: Case Series with Review of Literature

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Abstract

Background:

Inflammatory bowel disease(IBD) affects women in their reproductive years with severe disease associated with maternal morbidity and adverse fetal outcomes

Methodology and Results:

We report our experience of managing pregnant women with IBD in South India. Of the five patients with IBD and 8 pregnancies, 2 presented with active severe disease during pregnancy and were treated with steroids and azathioprine. One developed chorioamnionitis and the other metabolic complications. All except 1 pregnancy required operative delivery by LSCS or instrumental delivery. The mean GA at delivery was 38+5 weeks with a mean birth weight of 2.93kg.

Conclusion:

Pregnancy outcomes in IBD are dependent on the disease activity status at conception. Diagnosis of IBD in pregnancy is a challenge as full length colonoscopy and CT imaging is not feasible. Chorioamnionitis is a complication associated with IBD, probably due to immunosuppressive drugs. There were no neonatal complications.

Introduction:

Inflammatory Bowel Disease (IBD) is an emerging disease in the tropics with improving socioeconomic status and change in dietary practices and worsening economic disparity.

Infective diarrhea is the commonest reason for an acute episode of altered bowel symptoms in India. However, some of these infections can persist for more than 2 weeks, and given the high burden of infections in the tropical regions delay the diagnosis of inflammatory disorders. India has also a high burden of chronic infectious diseases such as tuberculosis and chronic amebiasis that can mimic clinical presentation to Crohns disease that affect the ileocecal region.

In European countries, the incidence rates of Ulcerative Colitis (UC)and Crohn's Disease (CD), are 10.4/100 000 and 5.6/100 000 per year, respectively(1).Epidemiological studies from India(2)(3) have reported a prevalence rate of 42.8–44.3/100,000, and a crude incidence rate of 6.02/100 000 population. Access to clean drinking water was an independent risk factor for developing CD (4).

Both CD and UC affect women in the reproductive age group. Around one in four women diagnosed to have IBD become pregnant(5). Hence, it is important to understand the effects of IBD on pregnancy and vice versa for treatment of pregnant women with IBD especially in a tropical country with high infectious disease load. Women with IBD may choose to avoid pregnancy or discontinue their medications during pregnancy.

Pregnant women are less likely to be subjected to invasive investigations like colonoscopy to diagnose CD. Non-invasive tests like fecal calprotectin can be falsely positive in tuberculosis (6). Diagnostic delay in IBD is associated with poorer outcomes and increased risk of requiring surgery(7).

Population-based case control studies have reported no increase in still birth, neonatal death or spontaneous abortion(8) but is associated with premature births and low birth weight infants (9). Maintaining remission before pregnancy with appropriate medications offsets the risks of disease flares. These effects in a tropical country have not been studied.

Methodology:

We did a retrospective case series of patients with IBD admitted for delivery in a tertiary care university teaching hospital in India with 15000 deliveries per year from 2012–2018. The clinical details, endoscopy findings, histopathology findings, therapy given and pregnancy maternal and fetal outcomes have been summarized in Table 1 and 2.

Table 1
Baseline Characteristics

	Case 1	Case 2	Case 3	Case 4	Case 5
Diagnosis	Ulcerative Colitis	Ulcerative Colitis	Ulcerative Colitis	Crohn's Disease	Ulcerative Colitis
Clinical presentation	Not known	3 months of small volume loose stools with fresh blood 10–15 times a day with lower abdominal pain and generalized weakness	1 month of small volume loose stools with blood and recurrent uveitis	3 months of intermittent colicky abdominal pain and tenesmus with increased frequency of stools; significant loss of weight and appetite, abdominal distension and pedal oedema for 3 weeks. grade III clubbing	25days of large bowel bloody stools with no weight gain
Time of diagnosis	6 years prior to first pregnancy	3 years prior to first pregnancy	During pregnancy 12weeks GA	7 years prior to pregnancy	During pregnancy 19 + 3weeksGA
Basis of diagnosis	Unknown	Colonoscopy: grade III proctitis rectal biopsy: moderate chronic ulcerative proctitis with moderate to severe cryptitis	Rigid proctoscopy which showed multiple rectal ulcers and rectal erythema. Rectal biopsy; mild to moderate chronic active proctitis with crypt elongation, crypt disarray and mild cryptitis	Ileal resection histopathology showing deep mucosal ulceration, polyps and discrete epitheliod granulomas	Rigid sigmoidoscopy: diffuse colonic erythema and erosions. Biopsy: moderate active colitis with moderate cryptitis and crypt abscesses
Treatment received	Oral Mesalamine 2g twice daily	Mesalamine, Azathioprine, Sulfasalazine and Steroids	Mesalamine enema, oral sulfasalazine, Azathioprine, Steroids	Mesalamine Small bowel resection	Mesalamine – oral and rectal, steroids, Sulfasalazine

Table 2
Pregnancy outcomes

1st Pregnancy					
Age at the time of pregnancy (years)	31	34	28	29	30
Disease activity at the time of pregnancy	Quiescent	Quiescent	Active severe disease	Quiescent	Active severe disease
Treatment given during pregnancy	Oral Mesalamine 2g twice daily	Mesalamine	Mesalamine enema, oral sulfasalazine, Azathioprine, Steroids	Mesalamine	Mesalamine – oral and rectal, steroids, Sulfasalazine
Gestational age at time of delivery (weeks)	40 + 5	38 + 5	38 + 2	37 + 1	40
Mode of delivery	Low forceps for prolonged 2nd stage of labour	LSCS for IUGR and NRFS	LSCS for failed induction	LSCS for breech presentation and PROM	Normal vaginal delivery
Maternal complications	Nil	IUGR	Chorioaminionitis	PROM, Chorioamnionitis	Gestational diabetes, severe pre-eclampsia
Foetal complications	Nil	Nil	Nil	Nil	Nil
Birth weight(kg)	3.21	2.32	2.76	2.48	2.97
Apgar at 1and 5 mins	Apgar 9 and 10	Apgar: 9,10	Apgar: 9,10	Apgar: 9,10	Apgar: 9,10
2nd Pregnancy					
Age at the time of pregnancy	34 years	37 years		31 years	
Disease activity at the time of pregnancy	Quiescent	Active disease after stopping Mesalamine		Quiescent	
Treatment given during pregnancy	Mesalamine	Mesalamine – oral and enema		Mesalamine	

1st Pregnancy				
Gestational age at time of delivery (weeks)	40 + 3	37 + 3		37 + 1
Mode of delivery	Vacuum delivery for prolonged 2nd stage of labour	LSCS for doubtful scar integrity		LSCS in view off previous LSCS
Maternal complications	Gastroenteritis in the post-partum period	Nil		Nil
Foetal complications	Nil	Nil		Nil
Birthweight (kg)	3.62	2.82		3.24
Apgar at 1 and 5 mins	Apgar 9 and 9	Apgar: 9,10		Apgar: 9,10

Results:

We present 5 patients with IBD having a total of 8 pregnancies. Four patients had UC and one had CD. The mean age at the time of diagnosis was 27.2 years. The mean age at the time of first childbirth in these women with IBD were 30.4 years. Three of the patients were diagnosed to have IBD prior to pregnancy.

Two patients had active severe disease requiring steroids, azathioprine and aminosalicylates. One patient had flare of disease during pregnancy when she stopped her medications in the first trimester. All of the patients were on aminosalicylates. The patient with CD had history of small bowel resection and anastomosis prior to pregnancy; but none required surgical intervention for IBD during pregnancy.

The mean GA at delivery was 38 + 5 weeks. Seven pregnancies required operative delivery by LSCS or instrumental delivery. Two patients developed chorioamnionitis, one was on immunosuppression with azathioprine and steroids and the other had preterm premature rupture of membrane (PPROM). One patient developed infective gastroenteritis post-partum. All the infants had normal Apgar with a mean birth weight of 2.93kg.

Discussion:

In our series of patients, UC was more common than CD. Disease activity at the time of diagnosis has a strong association with maternal morbidity. Patients on treatment for IBD at time of being pregnant should be advised to continue the medications unless strongly contraindicated. Studies show that if IBD remains in remission during the duration of pregnancy, the risks of adverse maternal and fetal outcomes are similar to the

general population. They need to be monitored for infective complications in tropical countries with high infectious burden.

Diagnosis during pregnancy is challenging as CT scan is contraindicated and a complete colonoscopy is associated with increased risk. MRI abdomen, limited colonoscopy or flexible sigmoidoscopy can be used to in patients with high suspicion of IBD.

In a tropical country, with high prevalence of intestinal tuberculosis, enteric fever with ileal involvement and amoebiasis the diagnosis of IBD requires a more thorough work up as CD commonly involves the ileum and presents with granulomas. Delay in diagnosis and time to initiating immunosuppression is frequent. The diagnosis of inflammatory bowel disease should be considered in any patient with chronic diarrhoea, prolonged blood-stained stools and negative workup for infections. Early diagnosis and disease remission is essential to ensure good pregnancy outcomes.

Two of the patients had developed chorioamnionitis in this series. Of the patients with chorioamnionitis, one was on Azathioprine and steroids and the other had PPROM. Chorioamnionitis is not common in patients with IBD in pregnancy(10). Helpmen et al reported chorioamnionitis in an IBD patient on treatment with Azathioprine, but there are no large studies showing this correlation (11). However, in tropical countries with higher infectious disease burden the risk may be higher and requires further studies.

Conclusion:

IBD presents during the reproductive years. The diagnosis of IBD in pregnancy is a challenge and there can be delay in diagnosis. In a tropical setting, infectious causes like tuberculosis, enteric fever, amoebiasis and bacterial dysentery need to be ruled out. The pregnancy outcome with IBD is associated with the disease activity status at the time of pregnancy. Aminosalicylates are the mainstay of therapy and are relatively safe in pregnancy. Stopping of aminosalicylates during pregnancy can precipitate a flare and cause adverse outcomes. With quiescent disease, the maternal and fetal outcomes are comparable to a normal population. Active disease may be associated with higher incidence of maternal morbidity related to the disease, immunosuppression and higher LSCS rates. The risk of chorioamnionitis with IBD especially among women on immunosuppression needs to be explored in further studies.

Declarations:

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Research involving human participants

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References:

1. Binder V. Epidemiology of IBD during the twentieth century: an integrated view. Best Pract Res Clin Gastroenterol. 2004 Jun 1;18(3):463–79.
2. Khosla R, Willoughby CP, Jewell DP. Crohn's disease and pregnancy. Gut. 1984 Jan 1;25(1):52–6.
3. Sood A, Midha V, Sood N, Bhatia AS, Avasthi G. Incidence and prevalence of ulcerative colitis in Punjab, North India. Gut. 2003 Nov;52(11):1587–90.
4. Pugazhendhi S, Sahu MK, Subramanian V, Pulimood A, Ramakrishna BS. Environmental factors associated with Crohn's disease in India. Indian J Gastroenterol. 2011 Dec 1;30(6):264–9.
5. Heetun ZS, Byrnes C, Neary P, O'morain C. Review article: reproduction in the patient with inflammatory bowel disease. Aliment Pharmacol Ther. 2007;26(4):513–33.
6. Larsson, G., Shenoy, K. T., Ramasubramanian, R., Thayumanavan, L., Balakumaran, L. K., Bjune, G. A., & Moum, B. A. (2014). Faecal calprotectin levels differentiate intestinal from pulmonary tuberculosis: An observational study from Southern India.*United European gastroenterology journal*, *2*(5), 397–405. doi:10.1177/2050640614546947
7. Lee D, Koo JS, Choe JW, Suh SJ, Kim SY, Hyun JJ, et al. Diagnostic delay in inflammatory bowel disease increases the risk of intestinal surgery. World J Gastroenterol. 2017 Sep 21;23(35):6474–81.
8. Lindhagen T, Bohe M, Ekelund G, Valentin L. Fertility and outcome of pregnancy in patients operated on for Crohn's disease. Int J Colorectal Dis. 1986 Mar 1;1(1):25–7.
9. Mountifield RE, Prosser R, Bampton P, Muller K, Andrews JM. Pregnancy and IBD treatment: this challenging interplay from a patients' perspective. J Crohns Colitis. 2010 Jun;4(2):176–82.
10. Taleban S, Gundogan F, Chien EK, Degli-Esposti S, Saha S. Placental inflammation is not increased in inflammatory bowel disease. Ann Gastroenterol Q Publ Hell Soc Gastroenterol. 2015;28(4):457–63.
11. Helpman L, Pauzner D, Lessing JB, Kupferminc MJ, Gutman G. Chorioamnionitis associated with Crohn's disease and azathioprine treatment: a case report. J Med Microbiol. 2005 Aug;54(Pt 8):803–4.