Pregnancy outcomes in Chinese women with ulcerative colitis: A retrospective study of 23 pregnancies

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Abstract

Background: Although China has a large population and increasing incidence of ulcerative colitis (UC), data on pregnancy outcomes in women with UC are insufficient and the relationship between simple clinical colitis activity index (SCCAI) and pregnancy outcomes has rarely been studied. This retrospective study aimed to assess the relationship between SCCAI and pregnancy outcomes of Chinese women with UC and explore factors affecting pregnancy outcomes. Methods: Overall, 23 pregnancies of 18 patients with UC were included. The following factors were analyzed: SCCAI before and during pregnancy; basic conditions, comorbidities, and treatment before and during pregnancy; frequency and details of pregnancy-related complications; and mode of delivery. Clinical characteristics, disease condition, and treatment details were compared between patients with and without adverse pregnancy outcomes. Results: The SCCAI was significantly lower in the remission group than in the active group ($P < 0.001$), except in the second trimester, but no significant difference in recurrence/exacerbation rate was found. There were 18 live births (remission group, 15; active group 3; $P > 0.05$). No significant difference in the frequency and characteristics of pregnancy-related complications was noted between the two groups. Outcomes of 15 pregnancies were satisfactory, but the other eight cases had adverse pregnancy outcomes. Patients with adverse pregnancy outcomes had higher SCCAI in the second trimester than the patients without adverse outcomes ($P = 0.034$). Multivariate analysis showed no statistically significant risk factor for adverse pregnancy outcomes. Conclusion: Chinese women with UC can usually achieve favorable pregnancy outcomes under multidisciplinary management, and a higher SCCAI in the second trimester has a positive correlation with adverse pregnancy outcomes.

Background

Ulcerative colitis (UC) is a chronic, idiopathic colon inflammation whose incidence is increasing globally [1]. Women with UC of childbearing age are at a high risk of complications as pregnancy may cause a disease flare while UC itself may affect pregnancy and delivery outcomes [2-4]. Therefore, fertility management and pregnancy outcomes in UC patients of childbearing age are always important. Laboratory parameters of UC are inconsistent during pregnancy, while the application of invasive examinations, such as colonoscopy, is limited. Thus, the diagnosis of UC in pregnancy is more often based on clinical manifestations.

The simple clinical colitis activity index (SCCAI) is a purely clinical index to evaluate UC disease activity and has demonstrated good correlation with the disease stage [5, 6]. The incidence of UC in China is approximately 2/100,000 [7] and is higher in the southern area than in the northern region [8]. Although China has a large population and increasing incidence of UC, data on pregnancy outcomes in women with UC are insufficient and the relationship between SCCAI and pregnancy outcomes has rarely been studied. Thus, more relevant research is needed to provide evidence for the management of pregnancy in UC patients.

To address the aforementioned gap in research, this retrospective study aimed to analyze the pregnancy outcomes in Chinese women with UC, assess the relationship between SCCAI and pregnancy outcomes, and explore the factors affecting pregnancy outcomes.

Methods

Eighteen patients with UC and with 23 pregnancies admitted to our hospital between January 2014 and February 2019 were studied. The need for informed consent was waived due to the retrospective nature of this study. Patients were followed regularly in our hospital from the beginning of pregnancy until delivery. The following factors were evaluated in the 19 pregnancies with UC in remission (remission group) and four pregnancies with active UC (active group): SCCAI scores before and during pregnancy; pre-pregnancy and pregnancy status, comorbidities, and treatment; and frequency and details of pregnancy-related complications; and mode of delivery. Clinical characteristics and treatment details were compared between the 15 cases without adverse pregnancy outcome (normal group) and eight cases with adverse pregnancy outcomes (abnormal group).

The clinical characteristics of all patients with UC were examined 3 months before conception. The disease activity of UC was assessed by SCCAI as follows: bowel frequency (per day): 1–3, 4–6, 7–9, and > 9 (score 0–3, respectively); bowel frequency (nocturnal): 1–3 and 4–6 (score 0 and 1, respectively); urgency of defecation: nil, hurry, immediately, and incontinence (score 0–3, respectively); blood in the stool: no, trace, occasionally frank, and usually frank (score 0–3, respectively); general well-being: very well, slightly below par, poor, very poor, and terrible (score 0–4, respectively); and extracolonic features: score 1 per manifestation. The sum of the scores forms the SCCAI, the total score ranges from 0 to 19, and a higher score indicates more severe UC activity. SCCAI ≤ 2 represents UC remission, SCCAI ≥ 3 reflects an active phase, while SCCAI score 3 to 5, 6 to 11, or ≥ 12 represent mild, moderate, and severely active phases, respectively [5]. Patients with a mean SCCAI ≤ 2 within 3 months before conception were assigned to the remission group; otherwise, they were assigned to the active group.

In this study, adverse pregnancy outcomes included ectopic pregnancy, abortion, premature delivery, intrauterine/mid-term induction of labor, and low birth weight. The first, second, and third trimesters of pregnancy were defined as 13 weeks +6 days, 14 to 27 weeks + 6 days, and ≥ 28 weeks of pregnancy, respectively.

Statistical analyses

The t-test was used to analyze parametric variables, and the Chi-squared test was used to analyze nonparametric variables. Logistic regression analysis for potential risk factors of adverse pregnancy outcomes was conducted. P values < 0.05 were considered statistically significant. SPSS version 19.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

Results

Disease condition of UC

The average SCCAI scores before pregnancy and in the first, second, and third trimesters were 4.8 and 5.0, 5.0, and 6.3, respectively, in the active group and 1.2 and 1.7, 2.6, and 1.9, respectively, in the remission group. No significant difference in SCCAI was found between the two groups in the second trimester, whereas the SCCAI was significantly higher in the active group than in the remission group ($P < 0.001$) in the other trimesters (Table 1). The following therapeutic drugs were used before and during pregnancy: aminosalicylic acids (ASA), glucocorticoids, immunosuppressants, and anti-tumor necrosis factor α (TNF-α) monoclonal antibodies. No significant differences in the treatments were observed between the active and remission groups. However, the rate of glucocorticoid usage before pregnancy was significantly higher in the active group than in the remission group ($P = 0.032$). The remission group had two cases of UC recurrence (10.5%), and no exacerbation was found in the active group; no significant difference was noted between the two groups. In addition, no significant differences in the age at disease onset, disease duration, gestational age, and pre-pregnancy comorbidities between the remission and active groups were found (Table 2).

Frequency of pregnancy-related complications and adverse pregnancy outcomes

Among the 23 pregnancies, the most common complication in the two groups was anemia (remission group vs active group, 21.1% vs. 50.0%, overall incidence 26.1%, $P > 0.05$); pregnancies with premature rupture of membranes (17.4%), gestational diabetes mellitus (13.0%), and group B streptococcal infection (4.3%) were successful delivery(detailed information of all 23 pregnancies can be found in the Supplementary Tables). No significant difference in pregnancy-related complications was observed between the two groups.

Adverse pregnancy outcomes occurred in 8 of 23 pregnancies (34.8%) [remission group, 6 (31.6%); active group, 2 (50%)]; no significant difference between the two groups was found (Table 3). Two cases of abortion occurred in the remission group (artificial abortion and spontaneous abortion, one case each). Only one patient had an ectopic pregnancy and received methotrexate therapy at 7 weeks of gestation, and one patient from the remission group had an unexplained fetal death in the 17th week of gestation. Mid-term induction of labor was performed in a patient diagnosed with UC (initial onset type, pancolitis, severe type, active phase) for the first time in the second trimester. Eighteen pregnancies has successful delivery (78.3%). Among the patients with UC and live births, the most common adverse pregnancy outcome was low-birth-weight infants (3/18, 16.6%).

Factors affecting pregnancy outcomes and the mode of delivery

Of the 23 pregnancies, 8 (34.8%) had adverse pregnancy outcomes (abnormal group), while the outcomes in the other 15 cases (65.2%) were satisfactory (normal group). A comparison of the clinical features of the two groups revealed that patients with adverse pregnancy outcomes had higher SCCAI in the second trimester (P = 0.034) and longer disease duration (P > 0.05) than patients without adverse outcomes (Table 4). No significant difference in the duration of gestation, age at disease onset, pre-pregnancy SCCAI and those in other trimesters, and drug treatments was found between the two groups. Multivariate logistic regression analysis showed no statistically significant risk factors.

One case each of spontaneous abortion, artificial abortion, and ectopic pregnancy were observed, one patient had mid-term induction of labor, and one patient had stillbirth; all other pregnancies were successful (78.3%). The modes of delivery in the 18 successful pregnancies were vaginal delivery (8 cases) and cesarean section (10 cases); no significant difference between the remission and active groups was found.

Discussion

UC may increase the risk of preterm birth, low birth weight, birth defects, or cesarean section; however, no evidence supporting the hypothesis that inflammatory bowel disease increases perinatal mortality is currently available [4]. Moreover, these risks are associated with disease status as patients with active UC have a more pronounced risk of adverse pregnancy outcomes than patients in remission. Supporting this conclusion, in our study, patients with adverse pregnancy outcomes had higher SCCAI in the second trimester than those who had no adverse pregnancy outcomes. This also demonstrated that SCCAI did can truly reflect UC disease stage even in pregnant women. Some studies have shown that during the pregnancy, approximately one-third of the patients with UC were stable, one-third of the patients exacerbated, while in one-third of the patients, the disease went into remission [9]. A neonatal registration cohort study including 47,710 births in Sweden found that the adjusted odds ratios of preterm and low-birth-weight infants in women with UC flare were 2.72 and 2.10, respectively, and the risk of miscarriage increased by four times compared with that in patients in remission [95% confidence interval (CI) 1.2–13.9; P = 0.02] [3].

Pregnancy may cause UC flare, and its effect on the course of the disease depends on the disease state at the time of conception. Patients who are pregnant during the active period have a significantly higher recurrence rate than those who conceive during the remission period. Moreover, 55% and 29% of patients with active UC experienced recurrence at the time of conception and during remission, respectively, and the risk ratio was 2.0 (95% CI 1.5–3.0; P < 0.001) [2].

In our study, the recurrence/exacerbation rate was not significantly different between patients with UC remission and those with active UC (Table 1), which could be attributed to the strict disease management in the active group. The SCCAI during pregnancy in the remission and active groups showed an upward trend compared with the pre-pregnancy SCCAI, suggesting that pregnancy is associated with a certain risk of UC relapse or aggravation, which is consistent with the results of previous studies. In addition,

although the gestational SCCAI in the remission group increased compared with the pre-pregnancy SCCAI, it decreased in the third trimester; in the active group, a continuous increase, even in the late pregnancy period, was observed. Thus, pregnancy is desirable when the disease is in remission, and the Toronto Consensus suggested that a sustained remission for at least 3 months may be a favorable time for conception [10]. None of the two groups discontinued medications during pregnancy, and no significant difference in the frequency of pregnancy-related complication and adverse pregnancy outcomes was noted between the two groups, which suggests that the use of appropriate medications during pregnancy is essential in managing UC and is critical for obtaining a satisfactory pregnancy outcome.

Considering the medications before and during pregnancy, the European Crohn's and Colitis Organization guidelines indicate that 5-ASA, glucocorticoid, immunosuppressive agents, and anti-TNF-α monoclonal antibodies are safe during pregnancy and the benefits of controlling the disease are greater than the potential risks [11]. The Toronto Consensus also recommends that patients who take these drugs before pregnancy should continue to take them during pregnancy to maintain a stable condition [10]. One patient started receiving adalimumab before pregnancy until 12 weeks of gestation; although her newborn had a low birth weight (2460 g), no evidence of infection was found, which was consistent with the aforementioned guidelines. Hence, obstetricians, gastroenterologists, and gastrointestinal surgeons should patiently and thoroughly educate patients on the safety of the drugs and the effect of the disease activity on pregnancy, which could in turn help promote stability of the disease before and during pregnancy and achieve good pregnancy outcomes.

Moreover, patients with UC have an increased risk of adverse pregnancy outcomes, such as preterm birth and low birth weight, compared to the general population [4]. In our study, low birth weight was the most common adverse pregnancy outcome, which could be related to maternal anemia. Anemia was the most common manifestation in pregnant women with UC [12]. Moreover, a previous study showed a certain correlation between anemia in patients with UC and low-birth-weight infants [13], which is consistent with our results. In addition, no significant difference in the frequency of pregnancy-related complications and adverse pregnancy outcomes was noted between the two groups (Table 3); one case of artificial abortion and one case of labor induction were noted, and these cases resulted in a subjectively increased frequency of adverse pregnancy outcomes. The patient in our study underwent induction of labor because conservative treatment including systemic glucocorticoid administration was not effective, and the patient experienced acute massive gastrointestinal hemorrhage. She and her family members were strongly urged to terminate the pregnancy after they were informed about the potential adverse effects of the therapeutic drugs, surgery, and endoscopy on the fetus. After induction of labor, laparoscopic pancolectomy and ileostomy were successfully performed to control the gastrointestinal hemorrhage. Remission was achieved postoperatively with intravenous glucocorticoids combined with oral mesalamine and maintained by a combination of oral mesalazine and hydrocortisone. After 2 years, this patient conceived again and delivered a full-term live male baby vaginally (3240 g without any neonatal complication) after continuous monitoring and strict follow-up by obstetricians, gastroenterologists, and gastrointestinal surgeons. Except for mild anemia and premature rupture of membrane, no other serious

maternal complication was observed, suggesting that the maintenance of remission and optimal pregnancy management are vital for satisfactory pregnancy outcomes.

Our study showed no significant difference in the mode of delivery between the remission and active groups (Table 3). Nevertheless, the rate of cesarean section was high in the remission (40%) and active (66.7%) groups or in all patients with UC (44.4%), suggesting that UC may increase the risk of cesarean section, which is consistent with the finding in a previous study [4]. However, the selection of the mode of delivery remains controversial. UC is not an independent risk factor of cesarean section, and the patient's obstetric conditions have greater effect in the decision-making. Nevertheless, in patients with ileal pouch-anal anastomosis, cesarean section is recommended to terminate gestation and, thus, avoid sphincter and intestinal damage [14]; however, whether vaginal delivery increases the risks of sphincter and intestinal damage remains to be further established [15, 16]. Nonetheless, the mode of delivery in patients with UC must be discussed with obstetricians and gastroenterologists, should be based primarily on obstetric considerations, and should consider the patient's preference.

As mentioned previously, patients with adverse pregnancy outcomes had higher SCCAI in the second trimester than patients with no adverse pregnancy outcomes, suggesting that a higher SCCAI in the second trimester may be associated with adverse pregnancy outcome. A multivariate regression analysis found no statistically significant risk factors for adverse pregnancy outcomes, indicating that multidisciplinary collaboration in the management of pregnancy in patients with UC is vital to achieve satisfactory outcomes.

This retrospective study had some limitations. The patients were all regularly followed before and during pregnancy. Thus, selection bias was possible. Moreover, the small sample size may have increased the risk of type I errors. In addition, this study lacked data on the long-term outcomes of the offspring of the enrolled patients.

Conclusions

Chinese women with UC can usually achieve favorable pregnancy outcomes under multidisciplinary management. Moreover, a higher SCCAI in the second trimester has a positive correlation with adverse pregnancy outcomes. Altogether, this study provides some new information about pregnancy outcomes in Chinese women with UC. Nevertheless, studies with larger sample sizes and in different ethnic groups should be conducted to thoroughly evaluate the relationship between SCCAI and pregnancy outcomes and, thus, establish more effective management protocols for pregnant women with UC.

List Of Abbreviations

5-ASA: 5-aminosalicylic acid

SCCAI: simple clinical colitis activity index

TNF-α: tumor necrosis factor α,

UC: ulcerative colitis

Declarations

Ethics approval and consent to participate

The Ethics Committee of Peking Union Medical College Hospital approved this study. The need for informed consent was waived due to the retrospective character of the study. All the patients enrolled in this retrospective study received standard treatment in accordance with the clinical guildlines during the follow-up, without additional clinical trial and risk. Patient's name or other personal private information were eliminated in this study, only the clinical characters were used to analyze.

Consent for publication

Not applicable

Availability of data and materials

The authors confirm that the data supporting the findings of this study are available within its supplementary materials.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SJ L and JS G conceived and designed the study, wrote and manuscript. J H, and XX C collected clinical data and participated in statistical analysis. JT L and Y L participated in the design and coordination of the study. All authors read and approved the manuscript.

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Tables

Table 1: Clinical characteristics and disease condition of patients with UC

	Remission group (n = 19)	Active group (n = 4)	P value
Age of disease onset (years)*	24.6 ± 4.4 (17–31)	29.3 ± 7.1 (23–39)	NS
Duration of IBD (years)*	7.3 ± 3.6 (0–13)	5.8 ± 3.8 (2–11)	NS
Age of pregnancy (years)*	32.0 ± 3.9 (25–43)	35.0 ± 6.2 (30–44)	NS
SCCAI before pregnancy	1.2 ± 0.4	4.8 ± 1.5	< 0.001
Recurrence/exacerbation	2 (10.5%)	0	NS
SCCAI score during pregnancy			
First trimester	1.7 ± 0.7	5.0 ± 1.8	< 0.001
Second trimester	2.6 ± 2.5	5.0 ± 1.7	NS
Third trimester	1.9 ± 1.2	6.3 ± 1.5	< 0.001

Data are expressed as mean ± standard deviation.

Ectopic pregnancy was excluded from the second and third trimester SCCAI scoring, mid-term induction of labor and stillbirth were excluded from the third trimester SCCAI scoring.

IBD: inflammatory bowel disease, SCCAI: Simple Clinical Colitis Activity Index

* Minimum to maximum value

Table 2: Treatment in the remission and active groups

	Remission group (n = 19)	Active group (n = 4)	P value
Medications before pregnancy (y/n)	16/3	4/0	NS
5-ASA	15	4	NS
Corticosteroids	2	3	0.032
Immunosuppressants	1	1	NS
Anti-TNF-α monoclonal antibody	1	0	NS
Complications before pregnancy	4	1	NS
Hypothyroidism	3	1	NS
Surgical history of UC	1	0	NS
Medications in pregnancy (y/n)	15/4	4/0	NS
5-ASA	13	4	NS
Corticosteroids	2	2	NS
Immunosuppressants	1	1	NS
Biologics (anti-TNF-α monoclonal antibody)	1	0	NS

5-ASA: 5-aminosalicylic acid, TNF-α: tumor necrosis factor α, NS: not significant

Table 3: Adverse maternal and fetal events during pregnancy and the mode of delivery

	Remission group (n = 19)	Active group (n = 4)	P value
GDM	3	0	NS
GBS (+)	0	1	NS
PROM	4	0	NS
Anemia	4	2	NS
Abortion	2	0	NS
Induction of labor/stillbirth	2	0	NS
Preterm delivery	1	0	NS
Low birth weight	2	1	NS
Delivery method	15	3	NS
Cesarean section	6	2	NS
Vaginal delivery	9	1	NS

One or more events per patient occurred in some cases.

GDM, gestational diabetes mellitus; GBS, group B streptococcus; PROM, premature rupture of membrane; NS, not significant

Table 4: Clinical features of the normal and abnormal groups

	Univariate analysis			Multivariate analysis
	Normal group (n = 15)	Abnormal group (n = 8)	P value	Odds ratio
Disease stage (remission/active)	13/2	6/2	NS	
Recurrence/exacerbation	1 (0.7%)	1 (12.5%)	NS	
Age of onset (year)*	26.1 ± 3.2 (20–31)	24.1 ± 7.7 (17–39)	NS	
Duration of UC (year)*	6.4 ± 2.9 (2–12)	8.1 ± 4.6 (0–13)	NS	
Age of pregnancy (year)*	32.7 ± 3.7 (28–43)	32.3 ± 5.7 (25–34)	NS	
SCCAI before pregnancy	1.5 ± 0.9	2.4 ± 2.3	NS	
SCCAI during pregnancy				
First trimester	1.9 ± 1.0	3.0 ± 2.2	NS	
Second trimester	2.3 ± 0.9	5.0 ± 4.5	0.034	
Third trimester	2.5 ± 1.8	3.7 ± 3.8	NS	
Medications in pregnancy (y/n)	12/3	7/1	NS	
5-ASA	12	6	NS	
Corticosteroids	1	3	NS	
Immunosuppressants	0	2	NS	
TNF-α monoclonal antibody	0	1	NS	

Data are expressed as mean ± standard deviation.

UC, ulcerative colitis; SCCAI, Simple Clinical Colitis Activity Index; 5-ASA, 5-aminosalicylic acids; TNF-α, tumor necrosis factor α

*Minimum to maximum

Supplementary Table Legends

Table 1: Detailed information of the 23 pregnancies enrolled in this study

Table 2: Details of the medication and complications of the 23 pregnancies

Supplementary Files

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