



## Pregnancy and Irritable Bowel Syndrome

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Does pregnancy exacerbate gastrointestinal (GI) symptoms in women with functional bowel disorders, and irritable bowel syndrome (IBS) specifically? This question is relevant for a number of reasons. First, women of reproductive age represent a significant portion of patients with IBS. Second, there is evidence that reproductive cycling (i.e., menstrual cycle) influences symptom reports and bowel transit. This suggests that ovarian hormones, which are elevated in pregnancy, may contribute to GI symptoms. Third, little is known about effective treatment strategies for pregnant women with IBS. While there is some anecdotal information about amplification of symptoms during pregnancy, unfortunately there are limited clinical or laboratory data to validate such changes. This report is intended to address what is known about the potential role of pregnancy in symptoms of IBS.

First it is important to point out that to date there is no evidence that fertility is influenced by IBS. It is estimated that in the U.S. approximately 8–10% of couples are infertile. Whether women with IBS have fewer children than women without IBS is not known. Fear of symptom amplification with pregnancy or disruption in body image may be factors that contribute to the decision about whether to have children but these hypotheses remain to be tested.

The question of pregnancy amplification of IBS symptoms is derived from generic observations of gender differences in IBS. The past decade has seen a growing interest in the role of gender and basic physiologic differences that may account for clinical observations of patients with IBS. It is well known that in the U.S. as well as most westernized countries women seek health care services for IBS more commonly than men do. Indeed, approximately two-thirds of individuals with IBS are women. Although there are few differences in abdominal pain reports, women are more likely to report problems with constipation, intestinal gas, and bloating as compared to men [3]. In addition, women with IBS are also more likely to report extraintestinal symptoms or co-existing conditions such as fibromyalgia, chronic fatigue syndrome, and migraine

headaches. Although plausible explanations for these gender-related differences remain elusive several hypotheses exist including differences in motility and transit, pain sensitivity, central nervous system processing of peripheral sensory input, and autonomic nervous system regulation. In addition, psychological distress and stress may serve as important triggers in patients with IBS.

The study of these *etiologic mechanisms* [the processes that cause or contribute to the cause of diseases or conditions], while challenging in non-pregnant women because of natural fluctuations in hormones and intra-individual differences in cycle length, is even more difficult in pregnant women. The option of using invasive monitoring protocols is limited and symptomatic women experiencing nausea and vomiting are often reluctant to participate in studies that necessitate the insertion of tubes into the GI tract. As a result the data related to pregnancy and bowel function are extremely limited.

Upwards to a third of pregnant women experience increased constipation, particularly during the 3<sup>rd</sup> trimester[5]. Another third of women report an increase in stool frequency during pregnancy. There are at least two mechanisms by which pregnancy can influence bowel function. First, through the ovarian hormones estrogen and progesterone which are elevated throughout pregnancy. There are data to support the notion that these hormones influence various aspects of bowel function and may contribute to symptoms. Second, the growing fetus can place physical pressure on the bowel wall, however, this remains an unexplored phenomenon.

Despite the observation that many women report increased GI symptom distress (e.g., heartburn, nausea, constipation) in the early phase (i.e., first trimester) of pregnancy there have been few studies. In one study of pregnant women complaining of nausea during the first trimester, investigators using an external recording device (electrogastrography) observed stomach motility alterations (dysrhythmia) in 5 of the 8 women[6]. In this

same study non-pregnant women given estrogen plus progesterone or progesterone alone to mimic pregnancy hormone levels also demonstrated a slowing of gastric motility. Theoretically, decreases in gastric motility could be linked to slowed gastric emptying and contribute to sensation of fullness and nausea. However, other investigators have observed no change or increased gastric emptying in pregnant women.

A somewhat larger study (11 pregnant women) that involved multiple assessments during pregnancy and post pregnancy[1], using hydrogen breath tests, found that transit time was longer during the 3<sup>rd</sup> trimester as compared to postpartum observation. Interestingly the women reported more symptoms of *dyspepsia* during the first trimester when no differences in transit time or gastric emptying were noted. The fact that transit was decreased in the 3<sup>rd</sup> trimester but not the 1<sup>st</sup> raises the suggestion that differences were related more to physical factors (i.e., fetal growth) rather than hormone levels.

Progesterone and estrogen have been implicated in motility disturbances. The increased report of dyspepsia during the first trimester is ascribed to progesterone, which is thought to have a direct relaxation effect on the lower esophageal sphincter. In a recent review Richter outlines strategies for management of pregnancy-related dyspepsia beginning with a *step-up approach*[4]. Whether women with IBS (diagnosed by the presence of abdominal pain and alterations in bowel patterns) have increased dyspepsia or nausea and vomiting during the 1<sup>st</sup> trimester is not known.

There have been relatively few studies of pregnancy using animal models. Most animal studies have focused on specific effects of estrogen and progesterone on bowel wall muscle contractility. Taken together these studies demonstrate that gastric emptying and intestinal transit are decreased in rats in which the ovaries are removed (ovariectomized) when treated with estrogen, progesterone, or the combination of both as compared to controls. While estrogen and progesterone may influence bowel function, the question is what is the precise mechanism (e.g., via neural elements, enterochromaffin cells in the GI tract, or direct effects) on gut smooth muscle. At the same time, other pregnancy-related hormones such as relaxin may also contribute to decreasing intestinal transit.

It remains to be determined whether women who prior to pregnancy had constipation predominant symptoms are likely to experience an increase in symptoms related to overall slowing of transit associated with pregnancy. At the same time it could be asked whether women with diarrhea-predominant symptoms experience an improvement in symptoms during pregnancy.

Less is known about how estrogen and progesterone might modulate (decrease) pain sensitivity. Non-pregnant women have heightened somatic (skin and muscle) and visceral (intestinal) sensitivity relative to men. However, during pregnancy elevations in circulating levels of estrogen and progesterone produce gestational *antinociception* (increased tolerance to pain). This conclusion is based on a series of experiments with pregnant, pseudopregnant, and ovariectomized hormone treated animal models. These pain tolerance changes are related to changes that occur in spinal processing of sensory input from the periphery to the central nervous system. Such results would suggest that pain sensitivity would be reduced during pregnancy, perhaps reducing the severity of abdominal pain. However, there is little research related to IBS to determine whether abdominal pain sensitivity is diminished during pregnancy.

For many women pregnancy is a time of heightened stress and this may exacerbate underlying psychological distress conditions such as anxiety and depression. Again this is an area which remains poorly understood and in need of study.

### **Management**

Non-drug therapies for IBS including education, reassurance, and relaxation therapy are important steps in management of IBS symptoms during pregnancy. Understanding that slowed intestinal transit occurs during pregnancy for some women may help to alleviate associated anxiety over constipation. Non-drug therapies have been tested in non-pregnant women and found to be effective in reducing distress and possible symptom triggers. Dietary changes can also be considered safe for pregnant women. This might include additional fiber (e.g., fruits, vegetables, and grains) in those with inadequate fiber intake and reduction of gas-producing foods (e.g., beans, cabbage, legumes, cauliflower, broccoli, lentils, and Brussels sprouts) to reduce abdominal discomfort. Castor oil as a laxative should be avoided during pregnancy because of concerns related to premature uterine contraction[5]. Saline hyperosmotic cathartics can also cause problems secondary to sodium and water retention.

Current drug therapies for IBS are focused on specific symptoms or symptom complexes such as constipation, diarrhea, bloating, and abdominal pain. These therapies have been tested in non-pregnant subjects and thus their efficacy in pregnant women remains essentially unknown. At the same time concerns for fetal development and adverse maternal effects limit use of drugs for pain and diarrhea management. Similarly women should be instructed to avoid herbal therapies for IBS symptoms because many remain untested.

## Summary

In summary there is no scientific evidence to suggest that women with IBS are more likely to be infertile, have difficulties with pregnancy, or experience adverse outcomes related to their pregnancies. In addition there is no evidence that symptoms are worse following delivery. During pregnancy there are changes in bowel function (relaxation of lower esophageal sphincter and decreased intestinal transit) that are likely linked to increases in reports of heartburn and constipation. Such changes are likely associated with elevations in circulating levels of estrogen and progesterone.

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