Gastrointestinal Conditions during Pregnancy

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ABSTRACT

Pregnancy causes anatomic and physiologic changes in the gastrointestinal tract. Pregnant women with intestinal disease such as Crohn disease or ulcerative colitis pose a management challenge in clinical diagnosis, radiologic evaluation, and treatment secondary to potential risk to the fetus. Heightened physician awareness on possible etiologies such as appendicitis, diverticulitis, and rarely colorectal cancer is required for rapid diagnosis and treatment to improve maternal/fetal outcome. A multidisciplinary approach to evaluation is a necessity because radiologic procedures and treatment medications commonly used in nonpregnant patients may have a potential harmful effect on the fetus. The authors review several gastrointestinal conditions encountered during pregnancy and address presentation, diagnosis, and treatment of each condition.

KEYWORDS: Gastrointestinal, pregnancy, constipation, inflammatory bowel disease

Objectives: On completion of this article, the reader should be familiar with the management of gastrointestinal conditions that may occur during pregnancy.

Pregnancy causes anatomic and physiologic changes in the gastrointestinal (GI) tract, which result in common patient complaints of nausea, emesis, constipation, hemorrhoids, and gastroesophageal reflux. Some patients have underlying GI conditions such as Crohn disease or ulcerative colitis that may affect pregnancy outcome.

An acute abdomen during pregnancy poses a management challenge in clinical diagnosis, radiological evaluation, and treatment secondary to potential risk to the fetus. Heightened physician awareness on possible etiologies such as appendicitis, diverticulitis, and rarely colorectal cancer is required for rapid diagnosis and treatment to improve maternal/fetal outcome. A multidisciplinary approach to evaluation is a necessity because radiologic procedures and treatment medications commonly used in nonpregnant patients may have a potential harmful effect on the fetus. In this article, we will review some GI conditions encountered during pregnancy and address presentation, diagnosis, and treatment of each condition.

CONSTIPATION

Constipation is a common complaint of pregnant women secondary to the physiologic changes that accompany normal gestation. Investigators during the 1970s noted that the incidence of constipation in pregnancy ranged from 10 to 40%. More recent surveys have confirmed this variable incidence.[1–3] Ethical limitations of research in pregnancy have prevented a clear etiology and incidence of constipation during pregnancy to be determined. However, the GI responses to estrogen and progesterone with increased bowel transit time and

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uterine mechanical obstruction are considered major physiologic factors. Other causes include decreased maternal activity, decreased levels of motilin, increased colonic sodium and water absorption, and routine iron supplementation in the pregnant population.[4]

Education of the pregnant patient on the physiologic changes that occur to the GI tract during gestation may prove invaluable. Providing an explanation of the cause of constipation and advising simple ways to relieve the discomfort are usually adequate. Basic advice should include increased fluid and fiber intake, a moderate amount of daily exercise, and defecation after meals when colonic activity is the highest. Most patients' complaints of constipation can usually be relieved with an increase in dietary fiber, which is present in most cereals, especially bran.

For those who are unable to modify their activity or diet to experience relief, many benefit from meal supplementation with 4 to 6 tablespoons of bran, or another bulk forming agent such as psyllium, methylcellulose, or polycarbophil. Daily ingestion of these bulk-forming agents, along with 1 to 2 glasses of water, relieves constipation via increased fecal water content, decreased colonic transit time, and increased stool weight. Patients should be instructed that bulk-forming agents may take a few days to achieve their desired effects. Once desired results are accomplished, the amount of supplementation can be titrated to achieve continued relief throughout pregnancy.[5]

Probiotics (supplements containing "healthy bacteria") are being suggested more often in pregnant patients. These supplements can alter the flora of the colon and many patients notice an improvement in their bowel function. Multiple over-the-counter preparations are available. Prospective controlled studies in pregnant patients are limited, but these agents have little to no potential for harm, other than cost and compliance issues. Increasing experience will define any differences between products and the appropriate role for these supplements.

Osmotic and stimulant laxatives are second-line therapy when bulk-forming agents fail to achieve relief. They have the benefit of faster onset of action when compared with bulk-forming agents, but side effects may limit their long-term use. Hyperosmolar laxatives such as sorbitol and lactulose, increase fecal water content but may cause maternal electrolyte disturbances with long-term administration. Because hyperosmolar laxatives are indigestible sugars, they have the uncomfortable side effects of flatulence, bloating, and nausea, which may be intolerable during pregnancy. Furthermore, lactulose is best avoided in patients with diabetes and those requiring a low galactose diet because of its metabolites—lactose and galactose. Polyethylene glycol is an isomotic agent that retains water in the intestinal tract. At appropriate doses, it appears safe for long-term use. Stimulant laxatives such as bisacodyl, senna, and cascara have the fastest onset of action, but are associated with hypokalemia, hyponatremia, and colic.[5] In particular, bisacodyl is best tolerated as a rectal suppository secondary to its association with colic. The use of stimulant laxatives greater than three times per week is not recommended. Because of its association with preterm labor and fetal meconium passage, castor oil is best avoided as a laxative for pregnant women.[6] Many obstetricians routinely prescribe laxatives, such as sorbitol, to the postpartum patient because of defecation pain that may accompany a posterior vaginal laceration or episiotomy. Daily sorbitol is also commonly prescribed to patients who have had a cesarean section in an effort to decrease constipation associated with narcotic pain medication usage.

The likelihood of constipation resulting in fecal impaction during pregnancy is rare. Most patients who experience such an event have a predisposing condition, such as a neurologic injury.[7] Mechanical relief of an impaction is not common during pregnancy, but may be accomplished in the same manner as performed by a nonpregnant patient, which entails gentle digital force and fluid enemas.

HEMORRHOIDS

The increased incidence of constipation is a contributing factor to anorectal hemorrhoids, one of the more common and discomforting, GI conditions of pregnancy. About one third of pregnant women complain of hemorrhoids secondary to various contributing factors that include increased Valsalva force during defecation, a 30% increase in blood volume, progesterone-induced venous smooth muscle relaxation, and increased intraabdominal pressure from uterine growth.[4]

The need for treatment of hemorrhoids is usually determined by the type. Classically, hemorrhoids are divided into external (those that originate below the dentate line) and internal (those that originate above the dentate line). External hemorrhoids usually require no treatment unless thrombosis has developed. First-line therapy includes conservative measures to decrease the pain and facilitate clot resorption. Initial therapy should include stool softeners, topical analgesics, and warm sitz baths. If these therapies are unable to achieve relief, surgical excision under local anesthesia is preferred over clot incision and removal because of the high rate of clot recurrence.

Initial therapy for internal hemorrhoids in pregnancy targets decreasing the strain associated with defecation, particularly in those patients with constipation issues. First-line treatment includes increased fiber consumption, laxative administration, over-the-counter topical anesthetic medications (benzocaine) that decrease pruritus, and topical anti-inflammatory agents

(hydrocortisone). If conservative measures fail, in-office rubber band ligation, infrared coagulation, or injection sclerotherapy appear to be safe and effective during pregnancy. If office interventions fail to provide relief or a hemorrhoid is incarcerated or prolapsed, a surgical hemorrhoidectomy may be performed, rarely.[7]

APPENDICITIS

Appendicitis is the most common nonobstetric surgical procedure during pregnancy with an estimated incidence in pregnancy between 1:500 to 1:3000.[8–10] The findings are apparently no different than the age-appropriate nonpregnant population, and the incidence appears to remain steady in all three trimesters. As in the nonpregnant patient, the most common complaint is abdominal pain and nausea, the most common physical findings are abdominal tenderness and rebound, and the most common laboratory finding is leukocytosis. Though these commonalities are present, there is a notable increase in the rate of appendix perforation during pregnancy most likely secondary to a delay in diagnosis.[9] This delay is usually multifactorial and includes confounding factors such as imaging delay, abnormal location of abdominal pain, hesitancy of surgery team to proceed with an operative procedure, and the necessity for fetal evaluation prior to surgical intervention.

The most common diagnostic modality utilized in the evaluation of a pregnant patient suspected of having appendicitis is ultrasonography, using a graded compression technique. The benefits of ultrasonography include noninvasive technique, inexpensive cost, and freedom from ionizing radiation exposure. The parameters for diagnosis are the same as in the nonpregnant state and include a noncompressible or fluid-filled appendix that has an outer diameter greater than 6 mm. The sensitivity of the procedure can be limited in pregnancy because of increased body size, uterine size hindering adequate visualization, and appendix displacement by uterine growth. Sensitivities ranging from 65 to 100% have been reported in pregnancy.[11] As in the nonpregnant patient, if clear visualization of the appendix cannot be achieved, the diagnosis of appendicitis cannot be excluded and further diagnostic imaging is indicated.

Second-line imaging techniques for evaluation of appendicitis in pregnancy include computed tomography (CT) and magnetic resonance imaging (MRI). In the nonpregnant population, the first-line assessment for appendicitis is typically a helical CT with a sensitivity and specificity reported as high as 98%.[12] Helical CT has lower ionizing radiation exposure compared with conventional CT. Radiation exposure during a helical CT of the abdomen and pelvis, at 300 mrad, is far below the cutoff of 50 rad, the level for concern of fetal teratogenicity.[13] Theoretically, the risk of organ malformation and childhood cancers does not approach even 1% with radiation doses below 10 rad. However, because many physicians are reluctant to proceed with CT scanning during pregnancy, MRI of the abdomen and pelvis for visualization of the appendix is now gaining in popularity. MRI during pregnancy has never been shown to have adverse effects on fetal health; however, its use in the diagnosis of appendicitis is limited in both pregnant and nonpregnant patients. Preliminary studies have shown favorable sensitivities, but are controversial because of their small size and retrospective nature. In both modalities, as in ultrasonography the presence of an appendix >6 mm is suspicious for appendicitis.[12] In CT imaging the presence of fat stranding or fluid collection in the area of the appendix should warrant concern.

During the past 30 years, general surgeons have transitioned from open appendectomy to laparoscopic appendectomy for nonpregnant and pregnant patients. Since the first laparoscopic appendectomy that was performed during pregnancy in 1980, many pregnant patients have been successfully treated with this procedure.[9] The advantages of a shorter hospital stay, less pain, and a faster return to daily activities have been documented. The probability of successful laparoscopic removal of the appendix is decreased with advancing gestational age secondary to an enlarging uterus, which may hinder adequate visualization of the appendix. Care should be taken to avoid uterine puncture with trochar insertion in the late second and third trimesters. Therefore, many surgeons will perform an open initial trochar placement in those instances. The risk of a bleeding trochar site resulting in a hemoperitoneum has been reported, but is a rare complication.

With respect to fetal loss associated with appendicitis, most of the risk arises from the inflammatory response to rupture of the appendix with subsequent peritonitis as opposed to the operative procedure itself. Preterm labor associated with the inflammatory pathway is well established in the obstetrical literature. Inflammation is responsible for about a 10% fetal loss rate in pregnant women with peritonitis.[14] Additionally, appendiceal rupture rates are three to four times higher in the pregnant versus nonpregnant population.[15] Because of these comorbid factors, many maternal–fetal medicine specialists recommend perioperative antibiotic therapy, such as a second-generation cephalosporin, even in those patients that do not have a grossly ruptured appendix at the time of surgery. Furthermore, a 24- to 48-hour course of a nonsteroidal anti-inflammatory agent such as indomethacin should be considered to prevent the onset of preterm labor.

DIVERTICULITIS/MECKEL'S DIVERTICULUM

The incidence of diverticulitis is well known to increase with advancing age. Though less than 5% of cases are

diagnosed before the age of 40, more women are delaying their child bearing until later in life, and the incidence during pregnancy is expected to increase. Over the past 20 years the incidence at our facility has been ~1 in 6000 pregnancies. The mechanism of diverticulitis is fecal obstruction of a diverticulum resulting in inflammation and risk for rupture. The inflammatory response may trigger preterm labor and delivery if not treated.

Because of its rare presentation in pregnancy there are no good defined protocols for diagnosis and treatment of diverticulitis during pregnancy. Imaging modalities should include those that are used in the diagnosis of appendicitis: ultrasonography, CT, and MRI. In the nonpregnant population, most cases of uncomplicated diverticulitis can be treated with antibiotic therapy and bowel rest. However, some of the routine antibiotics (e.g., quinolones) administered in a nonpregnant state are contraindicated during pregnancy and consultation with a maternal–fetal medicine specialist should be considered. Furthermore, if operative intervention is required, the decision for tocolysis or delivery prior to or during the intervention should be well defined.

The diagnosis of a Meckel's diverticulitis is exceedingly rare in the pregnant patient. Though Meckel's diverticulum has an incidence of 2% in the general population, a review of the literature in 2005 by Rudloff et al noted only 23 cases of Meckel's diverticulitis in pregnancy reported since 1949.[16] In the 23 cases, only 2 were correctly diagnosed prior to surgery. Over half were ruptured at time of surgery and 4 of the 23 mothers, all diagnosed in the third trimester, died. Additionally, three pregnancies were lost. Though unlikely to be diagnosed prior to surgery, one must keep this rare occurrence in their differential. As with any patient suspected of bowel perforation, timely imaging, aggressive antibiotics, and early operative intervention should be standard.

INFLAMMATORY BOWEL DISEASE IN PREGNANCY

Ulcerative colitis (UC) and Crohn disease (CD) are both chronic disorders collectively known as inflammatory bowel disease (IBD). IBD often affects young adults during their reproductive years. Patients with IBD will often seek counseling about issues such as inheritance, fertility, effects of pregnancy on the course of disease, and the use of medications during pregnancy and the postpartum period.

Infertility rates in patients with IBD are similar to rates in the general population; however, active disease may impact female fertility. Medications used to treat IBD have no effect on female fertility.[17,18] The course of IBD during pregnancy tends to be similar to that in the nonpregnant population if conception occurs during time of inactive disease.[19,20] Approximately one-third of patients will relapse during pregnancy, especially in the first trimester or the postpartum period.[19,21,22] If the disease is active at the time of conception, disease activity persists or worsens in approximately two-thirds of patients.[23–26] Patients should be counseled that optimal pregnancy outcomes occur when the patient's disease is stable or she has not experienced a flare for several months prior to conception. The patient should continue to be followed by her gastroenterologist throughout the course of pregnancy.

The majority of studies show that patients with IBD not requiring medications did not have an increased risk of congenital abnormalities, spontaneous abortions, and stillbirths when compared with non-IBD patients.[27,28] Studies in patients with IBD have shown variable outcomes in the incidence of preterm delivery. Active IBD during pregnancy may be associated with an increased risk of congenital malformations, spontaneous abortions, fetal growth restriction, low birth weight, preterm delivery, and stillbirth.[27,29,30] Severe UC requiring surgery may be associated with worse pregnancy outcomes.[31]

Imaging modalities that may be used for diagnosis include plain film x-rays, ultrasound, MRI, and CT scans. Flexible sigmoidoscopy may be necessary for evaluation, and studies have shown that these procedures are relatively safe to perform during pregnancy.[32,33] In a recent review of endoscopy during pregnancy, these studies suggested that an esophagogastroduodenoscopy (EGD), sigmoidoscopy, and endoscopic retrograde cholangiopancreatography (ERCP) should be performed when strongly indicated. There is insufficient data on colonoscopy during pregnancy to determine its safety; however, there are reports of the use of colonoscopy during pregnancy without complications or poor outcomes.[33]

Despite the use of dietary modifications or bulking agents, the patient may continue to experience symptoms. There are many medications used to treat IBD that have been studied during pregnancy. Patients should be counseled about the benefits, risks, and fetal effects, if any, of taking these medications during pregnancy.

Aminosalicylates used to treat IBD include sulfasalazine and mesalazine. Analyses of studies of sulfasalazine and mesalazine during pregnancy have not indicated any significant increased prevalence of congenital abnormalities, low birth weight, or poor pregnancy outcomes.[19,34–36] The use of sulfasalazine and mesalazine during lactation has been associated with diarrhea in infants; therefore, patients should use caution while breastfeeding.

Antibiotics have been commonly used in the treatment of IBD. Metronidazole and quinolones are often used when treating patients with active CD.

Meta-analyses of metronidazole use during pregnancy have not demonstrated an increase in the incidence of congenital malformation, abortion, or stillbirth.[37,38] Also, no adverse effects of ciprofloxacin have been reported[39–41]; however, its use during pregnancy should be avoided because fluoroquinolones have been associated with cartilage toxicity in animal studies and arthralgias/tendinitis in human studies.[42–44] Alternatively, macrolide antibiotics have not been associated with an increased incidence of congenital malformation, abortion, or stillbirth.

Corticosteroids are indicated for the treatment of moderate to severely active IBD. Corticosteroids have been associated with a higher rate of spontaneous abortion, low birth weight, and cleft palate in animal studies; however, this has not been demonstrated in human studies.[26,45,46] Budesonide is effective in patients with mild to moderately active Crohn's ileitis and/or right colon involvement. Limited studies of budesonide during pregnancy have been reassuring, but its systemic use during the first trimester may be associated with an increase risk in facial clefts.[47,48] Commonly used corticosteroids are safe to use during breastfeeding.

Patients with refractory CD unresponsive to the above treatments may be able to receive medications such as azathioprine (Imuran®, Prometheus Laboratories, Inc., San Diego, CA), 6-mercaptopurine (6-MP), methotrexate, or cyclosporine. Based on human studies, azathioprine or its active metabolite 6-MP are considered unlikely to increase the risk of congenital anomalies after exposure, although one study found an increase in atrial or ventricular septal defects.[49–51] Neonatal anemia, lymphopenia, and thrombocytopenia have been observed among infants born to women treated with azathioprine during pregnancy. There is insufficient safety data on the use of azathioprine or 6-MP during breastfeeding; therefore, breastfeeding is not recommended while taking these medications. Methotrexate is a folic acid antagonist and hence is teratogenic. Methotrexate is contraindicated and not recommended for use during pregnancy.

Moderate to severe refractory UC patients may be candidates for colectomy or cyclosporine therapy. The use of cyclosporine in pregnant patients with steroid refractory UC may be beneficial when compared with surgical treatment.[52–55] Surgery in this setting may be associated with an increased risk of stillbirth.[53] Cyclosporine therapy has not been associated with an increased risk of congenital malformations in both animal studies and human case reports; however, its use may be associated with an increased risk of low birth weight and preterm delivery.[56–61] Nephrotoxicity, a drug side-effect in adults, has been identified in animal offspring exposed prenatally to cyclosporines. Breastfeeding is not recommended during cyclosporine treatment. Infliximab (Remicade®, Centocor, Inc., Horsham, PA) may be indicated for the treatment of moderate to severe refractory or fistulizing CD. A limited number of patients who have had infliximab exposure during pregnancy include normal outcomes.[62,63] This includes a 2004 analysis of the infliximab safety database including 96 pregnancies with no increased risk of adverse outcomes detected in this limited population.

Performing surgery for IBD during the course of pregnancy has been associated with a high rate of spontaneous abortions and stillbirths.[64–67] Although surgery has been successfully performed during pregnancy, active IBD primarily should be treated medically. Surgical intervention should be reserved for significant emergencies including severe fulminant colitis, toxic megacolon, perforation, obstruction, or hemorrhage.

The majority of studies show that patients with IBD off medications did not have an increased risk of congenital abnormalities, spontaneous abortions, and stillbirths when compared with non-IBD patients. Studies in patients with IBD have shown variable outcomes in the incidence of preterm delivery. Active IBD during pregnancy may be associated with an increased risk of congenital malformations, spontaneous abortions, fetal growth restriction, low birth weight, preterm delivery, and stillbirth. Severe UC requiring surgery may be associated with poor pregnancy outcomes.

Imaging modalities that may be used for diagnosis include plain film x-rays, ultrasound, MRI, and CT, and flexible sigmoidoscopy. Studies have shown that these procedures are relatively safe to perform during pregnancy. In a recent review of endoscopy during pregnancy, the investigators suggested that EGD, sigmoidoscopy, and ERCP should be performed when strongly indicated. There is insufficient data on colonoscopy during pregnancy to determine its safety, but there are reports of the use of colonoscopy during pregnancy without complications or poor outcome.

Despite the use of dietary modifications or bulking agents, the patient may continue to experience symptoms. There are many medications used to treat IBD that have been studied during pregnancy. Patients should be counseled about the benefits, risks, and fetal effects, if any, of taking these medications during pregnancy.

Aminosalicylates used to treat IBD include sulfasalazine and mesalazine. Analyses of studies of sulfasalazine and mesalazine during pregnancy have not indicated any significant increased prevalence of congenital abnormalities, low birth weight, or poor pregnancy outcomes. Also, these medications have not shown an increased risk of kernicterus in infants. The use of sulfasalazine and mesalazine during lactation has been associated with diarrhea in infants, and patients should use caution while breastfeeding.

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Patients with UC should expect normal labor and delivery. Cesarean delivery should be performed for usual obstetric indications. Patients who have undergone ileal pouch-anal anastomosis (IPAA) can deliver vaginally without compromising anastomotic integrity.[68] Patients with active perianal involvement or the presence of an ileoanal pouch may be offered an elective cesarean delivery. There is a high rate (17.9%) of developing perineal involvement after vaginal delivery, usually with episiotomy, especially in patients with Crohn disease and no preexisting perineal involvement.[69] The use of episiotomy should be avoided in patients with IBD.

COLORECTAL CANCER

The incidence rate of cancer in pregnancy has been reported to range from 0.07 to 0.1%.[70] Colorectal cancer is one of the three most common types of cancer in women and can present in women of childbearing age especially if there is a genetic predisposition.[71] Women have a lifetime risk of colon cancer of 1 in 17 and the risk for development before age 40 is ~1 in 2000.[71] The mean age of women with colon cancer during pregnancy has been reported as 31 years of age with a range of 16–48 years.[72] Colorectal cancer during pregnancy is rare with an incidence of ~0.008% (1 in 13, 000 pregnancies).[73–75]

Diagnosis and treatment of colorectal cancer during pregnancy is challenging secondary to overlapping signs and symptoms of cancer and pregnancy. Those signs and symptoms include rectal bleeding, nausea, vomiting, abdominal pain, weight loss, anemia, abdominal mass, and altered bowel habits such as constipation.[72] Because these symptoms are similar to normal symptoms of pregnancy, there is usually a delay in diagnosis and treatment of colorectal cancer during pregnancy. Persistent rectal bleeding or rectal passage of tissue at the time of delivery is an ominous sign of colorectal cancer and should be fully evaluated.[70] When discovered during pregnancy, most cancers arise from the rectum compared with the nonpregnant state when most cancers arise from the extra pelvic colon.[76]

Usually colon cancer is detected in its advanced stages secondary to late diagnosis during pregnancy. Bernstein et al reviewed 41 patients with colorectal cancer during pregnancy and observed that all patients had stage II or greater disease. Colon obstruction, perforation, and metastasis are more frequent in pregnant women with colon cancer than the average population. A possible cause is the immunosuppressive state of pregnancy.

Colorectal cancer carcinogenesis and its relation to pregnancy is not well understood. Some investigators have demonstrated that ~20 to 54% of colon cancers have estrogen receptors (Ers),[77] whereas others have demonstrated progesterone receptors (PgRs), which may be stimulated by the estrogen and progesterone produced during pregnancy. Data pertaining to the role of these hormones in the etiology and progression of colon cancer are limited and conflicting.

The diagnosis of colorectal cancer in a nonpregnant patient entails the tumor marker serum carcinoembryonic antigen (CEA), abdominal imaging, and endoscopy with biopsy. Colonoscopy is the preferred procedure to confirm diagnosis; however, pregnancy is a relative contraindication. With endoscopy, there is the risk for fetal exposure to potential teratogenic medications, uteroplacental insufficiency with maternal hypoxia or hypotension, and the risk for placental abruption with the mechanical pressure to the uterus.[78] With informed patient consent, the procedure may be performed with a possible reduction in risk with the use of meperidine in place of benzodiazepines, maternal oxygen administration, fetal surveillance, and gentle abdominal compression.[74,79,80]

Because most cases of colorectal cancers during pregnancy are rectal carcinomas, if the lesion is confined to the distal colon, a flexible sigmoidoscopy (preferably without endoscopic medications) may be performed as an alternative to colonoscopy during pregnancy. One review showed that ~86% of colorectal cancers in pregnancy are below the peritoneal reflection.

CEA levels have been used during pregnancy for the diagnosis, monitoring, and prognosis of colorectal cancer. Unfortunately, CEA levels tend to be normal or slightly elevated during pregnancy and are not considered a useful screening tool with a low sensitivity and specificity.[76]

Abdominal CT imaging also assists in staging of colorectal cancer, but is relatively contraindicated in pregnancy secondary to the fetal risk with radiation exposure.[70,76] Abdominal ultrasonography is a reasonable alternative to CT especially for detection of hepatic metastases with a sensitivity of 75%. However, because of the gravid uterus, its role may be limited in evaluation of the pelvis. MRI without contrast may be another alternative as well, but experience is limited at this time.[76]

A multispecialty team should be involved in treatment during pregnancy and include the specialties of maternal–fetal medicine, surgical oncology, colon and

rectal surgery, medical oncology, gastroenterology, neonatology, and obstetrics anesthesia. Management is individualized and dependent on various factors that include maternal age, patient's desire for future fertility, gestational age at diagnosis, and cancer stage. Surgery is the primary therapy for colon and rectal cancer outside of pregnancy. The treatment goal is to implement therapy as soon as possible for the mother and balance this with delivery of the fetus at a gestational age that is optimal for neonatal outcome.

Treatment during pregnancy is complex and is based on the gestational age of the fetus, tumor stage, need for adjuvant chemotherapy, and if elective or emergent surgery is indicated. If diagnosis is made at less than 20 weeks gestation, the recommendation is discontinuation of the pregnancy followed by surgical resection of the tumor secondary to the controversial data regarding risk to the pregnancy with surgery.[81] Low anterior or abdominoperineal resection has been performed up to 20 weeks gestation without disturbance of the gravid uterus. Colon cancer diagnosis is rarely made prior to 20 weeks gestation; hence, there is limited data on fetal outcome after surgical resection.

If colon cancer is diagnosed after 20 weeks gestation, resection of the tumor may be delayed until after delivery of the infant with maternal risk of tumor progression.[70,81] The ultimate goal is to achieve fetal lung maturation; nevertheless, delivery may vary from 28 to 32 weeks gestation based on a multispecialty team decision. If bowel obstruction develops during the pregnancy, the recommendation for management is dependent on the gestational age. If found early in the pregnancy, tumor resection with or without anastomosis is recommended. If found later in the pregnancy, the recommendation is for a colostomy followed by tumor resection soon after delivery of the infant.

Ovarian metastasis affects 3 to 8% of nonpregnant women with colorectal cancer: a prophylactic bilateral oophorectomy is performed at the time of tumor resection. About 25% of pregnant women with colorectal cancer will have ovarian metastases.[82–86] If a tumor resection is performed during pregnancy, prophylactic ovarian removal may be deferred secondary to the possible risk for a spontaneous abortion, especially in the first trimester. Bilateral oophorectomy is performed during pregnancy if there is evidence of invasion.

Adjuvant chemotherapy has been shown to improve the survival rate by 5 to 10% for stage II or III colorectal cancer. Chemotherapy is not recommended during the first trimester of pregnancy, but may be administered in the second or third trimesters with close maternal/fetal surveillance. The recommended therapeutic agent is 5-fluoruracil (5-FU) which is an inhibitor of DNA synthesis. Some investigators have suggested a possible risk for teratogenicity associated with 5-FU.[87] Other new chemotherapeutic agents (e.g., irinotecan, capecitabine, and oxaliplatin) are available, but they are pregnancy category D classification.[70,74]

Adjuvant radiotherapy is recommended for Duke's B2 and C rectal cancers. Radiation treatment of the pelvis is not recommended during pregnancy and is usually delayed until after delivery.

The delivery mode is controversial, but vaginal delivery seems to be the preferred route.[74,81] Outside the normal obstetrical indications for cesarean section, indications for an operative delivery in colorectal cancer patients include a tumor along the anterior rectal wall secondary to increased risk for tumor bleeding with vaginal birth pressure, birth canal obstruction by tumor, or when surgical tumor resection is planned during the same surgery. Recently, there has been a move toward vaginal delivery for women with rectal carcinoma even with an unripe cervix requiring a cervical ripening agent.

Pregnant women with colorectal cancer tend to have a poor prognosis mainly secondary to delayed diagnosis. Five-year cancer survival is the same for pregnant women as compared with the general population. A large clinical study of pregnant women and survival from rectal cancer reported 83% for Duke's stage B, 27% for Duke's stage C, and 0% for Duke's stage D. With respect to survival of pregnant patients with colon cancer, a Duke's stage B is 75%, Duke's stage C is 33%, and Duke's stage D is 0%.[72,88] Woods et al reported that in his series only 25 of 32 pregnancies in women with colorectal cancer had healthy live-born infants with the deaths attributed to intrauterine demise and prematurity.[89] Patients tended not to survive beyond 5 years.

CONCLUSION

Colorectal cancer is rare during pregnancy, but with expected poor outcome. Treatment during pregnancy poses significant ethical, religious, and scientific challenges. Because there are no absolute guidelines, therapy should be individualized and defined by a multidisciplinary team that considers the best management for both the patient and her fetus. Improvement in prognosis for this high-risk patient population should focus on an increased awareness by primary care physicians and obstetricians of significant GI symptoms of a pregnant woman with early referral to a gastroenterologist or colorectal surgeon for prompt evaluation, detection, and treatment of colon cancer.

SUMMARY

Abdominal symptoms are common in pregnancy, and the differential diagnosis is extensive, including obstetric, GI, and other disorders that may be unrelated to pregnancy. Physiologic adaptations in pregnancy may alter clinical presentations. The patient's history, physical examination, laboratory data, and radiologic

findings may assist in identifying the diagnosis. Abdominal ultrasound is first recommended, although MRI or CT may be used if necessary. Laparoscopy, EGD, and sigmoidoscopy can be performed during pregnancy when strongly indicated. Most medications appear to be relatively safe to the fetus and can be used when benefits to the mother outweigh potential fetal risks. A multidisciplinary approach is often necessary to maximize maternal and fetal benefit when managing GI disorders in pregnancy.

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