

Recent trend of acute appendicitis during pregnancy

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Abstract

Purpose We report the clinical presentation, management and outcomes of 33 patients who underwent surgery for acute appendicitis during pregnancy between April 1997 and March 2011.

Methods Several variables were compared between these 33 patients (pregnant group, $n = 33$) and non-pregnant females aged 20–40 years who underwent an acute appendectomy during the same period (control group, $n = 124$).

Results No significant differences were found between the two groups in terms of the type of anesthesia, operative method, duration of surgery, pathology, duration of antibiotic use, and incidence of surgical site infection, except for a higher frequency of pararectal incision performed and higher leukocyte counts in the pregnant group ($P < 0.01$). Tocolytic agents were administered to 17 patients (52 %). Preterm labor occurred in 10 patients (30 %), one of whom experienced preterm delivery.

Conclusions These results suggest that acute appendicitis during pregnancy can be managed successfully without fetal loss.

Keywords Acute appendicitis · Pregnancy

Introduction

Acute appendicitis is the most frequent extrauterine indication for laparotomy during pregnancy [1]. Physical and anatomical changes caused by pregnancy contribute to a delay in the diagnosis and treatment of appendicitis, possibly leading to the increased risk of fetal and maternal mortality. A decrease in the number of obstetricians has recently become a serious social issue in Japan. In addition, little is known about the management of acute appendicitis during pregnancy under such medical conditions. The purpose of this study was to elucidate the clinical presentation, management and outcomes in patients who underwent surgery for acute appendicitis during pregnancy in our hospital, which has a special center for reproducible and maternal-fetal high-risk medicine.

Patients and methods

Patients

The case records of all females who underwent surgery for acute appendicitis during pregnancy between April 1997 and March 2011 were reviewed and analyzed. The personal data evaluated included gynecological factors (gestational age, use of tocolytic agents, preterm labor, and preterm delivery), as well as factors associated with the diagnosis and management of appendicitis. Gestational age was categorized as the first (0–15 weeks), second (16–27 weeks), or third trimester (28 weeks and beyond). Several variables were compared between the pregnant females who underwent an appendectomy [pregnant group (PG)] and non-pregnant females who underwent surgery for pathologically proven acute appendicitis, matched according to age

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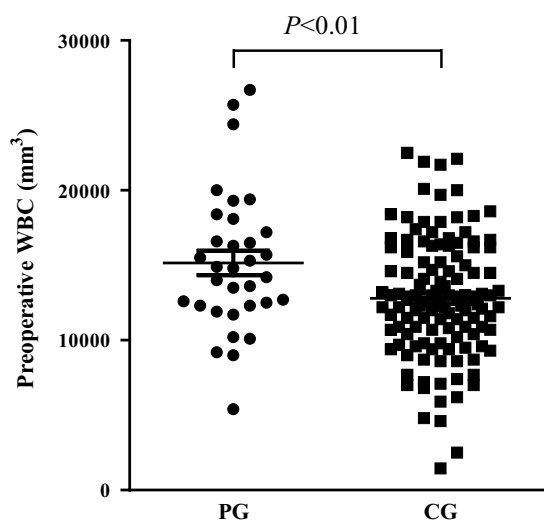


Fig. 1 Preoperative white blood cell (WBC) counts in the pregnant group (PG, $n = 33$) and control group (CG, $n = 124$)

with the pregnant group during the same period [control group (CG)].

Statistics

Continuous data are expressed as medians and ranges. A comparison of continuous or nominal variables was performed using the Mann–Whitney U test or Fisher’s exact probability test wherever appropriate. P values less than 0.05 were considered to be statistically significant.

Results

Preoperative factors

A total of 33 pregnant females, aged 19–34 (median 28) years, underwent an appendectomy, and the diagnosis of acute appendicitis was verified histologically in all cases. During the same period, a total of 770 deliveries were performed in our hospital. The gestational age was the first trimester in 14 patients, the second trimester in 17 patients, and the third trimester in two patients. Pain in the right lower quadrant of the abdomen was the most common presenting symptom regardless of the gestational age (53.3 % in the first trimester, 60 % in the second trimester, and 50 % in the third trimester; $P = 0.64$). Other locations of pain included the right upper quadrant, mid abdomen, epigastric region, and a combination of these locations. The presence of rebound and guarding on abdominal examination was documented in nine patients.

The preoperative white blood cell (WBC) count in the PG ($n = 33$) was significantly higher than that in the

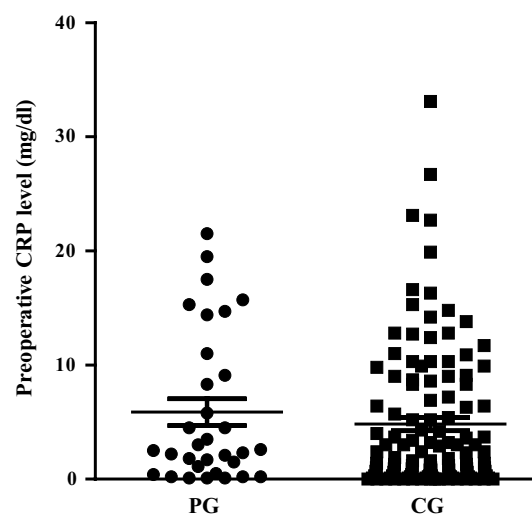


Fig. 2 C-reactive protein (CRP) levels in the pregnant group (PG, $n = 33$) and control group (CG, $n = 124$)

CG ($n = 124$) (median 15,151 and 12,797, respectively, $P < 0.01$) (Fig. 1), although the C-reactive protein (CRP) level was not significantly different between the two groups ($P = 0.81$) (Fig. 2). The median time from symptom onset to surgery was 30 (range 3–72) h in the PG and 49 (range 4–384) h in the CG ($P = 0.14$) (Table 1).

In the PG, abdominal ultrasonography (US) was performed in all cases to verify the presence of a tubular structure (suspicious appendix) below the painful region. Among the 33 patients, findings of acute appendicitis were detected in 24 (72.7 %). Abdominal computed tomography (CT) was performed in the remaining nine cases (27.3 %) whose appendix was not detected clearly by US. The CT findings of acute appendicitis were observed in all cases.

Surgical and pathological factors

The type of anesthesia, incision method, operative method, operative time, pathology of the resected appendix, and duration of antibiotic use are shown in Table 1. Endotracheal anesthesia was preferably adopted in seven patients (21.2 %) of the PG, while spinal anesthesia was adopted in 87 patients (70.2 %) of the CG ($P = 0.48$). A right pararectal incision was preferably selected in 16 patients (48.5 %) of the PG, while McBurney’s muscle splitting incision was selected in 92 patients (74.2 %) of the CG ($P = 0.003$). Diffuse peritonitis was not found in any patient of either group.

Appendectomy was the surgical intervention used in the PG, while four patients (3.2 %) of the CG underwent ileocecal resection because of aggressive local inflammatory findings ($P = 0.95$). The operative time ($P = 0.76$) and the pathological type proportions ($P = 0.58$) were

Table 1 Comparison of the clinical characteristics between the pregnant and control groups

| | Pregnant group (<i>n</i> = 33) | Control group (<i>n</i> = 124) | <i>P</i> value |
|--------------------------------------|---------------------------------|---------------------------------|---------------------|
| Preoperative WBC (mm ³)* | 15,151 | 12,797 | <0.01 |
| Preoperative CRP (mg/dl)* | 2.55 (0.1–21.5) | 1.6 (0.1–33.1) | 0.81 |
| Time to operation (h)* | 30 (3–72) | 49 (4–384) | 0.14 |
| Types of anesthesia | | | 0.8 |
| General anesthesia | 7 (21.2 %) | 36 (29 %) | |
| Lumbar anesthesia | 26 (78.8 %) | 88 (71 %) | |
| Incision method | | | <0.01 |
| McBurney | 15 (45.5 %) | 92 (74.2 %) | McBurney:others |
| Pararectus | 16 (48.5 %) | 27 (21.8 %) | |
| Median | 1 (3 %) | 4 (3.2 %) | |
| Transverse | 1 (3 %) | 1 (0.8 %) | |
| Operative method | | | 0.95 |
| Appendectomy | 32 (97 %) | 120 (96.8 %) | Appendectomy:others |
| Appendicectomy | 1 (3 %) | 0 (0 %) | |
| Ileocecal resection | 0 (0 %) | 4 (3.2 %) | |
| Operative time (min)* | 62.6 (20–120) | 62.6 (17–260) | 0.76 |
| Pathology of the resected appendix | | | 0.56 |
| Catarrhalis | 8 (24.2 %) | 24 (19.4 %) | |
| Phlegmonous | 12 (36.4 %) | 66 (53.2 %) | |
| Gangrenous | 13 (39.4 %) | 34 (27.4 %) | |
| Duration of antibiotic use (days)* | 3 (0–10) | 3 (0–7) | 0.35 |
| Surgical site infection | 2 (6.1 %) | 5 (4 %) | 0.98 |

* The data indicate the medians and ranges

not significantly different between the two groups. Two patients (6.1 %) of the PG and 12 (9.7 %) of the CG had perforated appendices.

All patients of both groups were given first or second generation cephalosporines, cepahamycin, or flomoxef twice daily perioperatively. The duration of antibiotic use was not significantly different between the groups ($P = 0.35$).

Two patients (6.1 %) of the PG developed wound infections, and five patients (4.0 %) of the CG developed intra-abdominal abscesses, of which two cases were associated with wound infection. There was no significant difference in the rate of surgical site infections between the two groups ($P = 0.67$).

As a tocolytic agent, ritodrine hydrochloride was administered to three patients (21.4 %) during the first trimester, 12 patients (70.6 %) during the second trimester, and two patients (100 %) during the third trimester. The median time of administration was 10 (range 1–44) days. Of these 17 patients, preterm labor occurred in 10 (30.3 %). A comparison of the clinical characteristics between the preterm labor and non-preterm labor groups among the 33 pregnant patients with acute appendicitis is shown in Table 2. The results indicate that the preoperative CRP was higher in the patients with preterm labor than in those with non-preterm

labor ($P = 0.003$). Furthermore, the pathological diagnosis in patients with preterm labor was significantly more severe than that in patients with non-preterm labor ($P = 0.02$). Preterm delivery occurred in a 29-year-old female during the second trimester the day after the appendectomy. She gave birth transvaginally to a boy, 812 g in weight in the 24th week of pregnancy. Immediately after birth, the newborn was intubated, requiring respiratory assistance for the following 227 days. The boy increased in weight to 2462 g and was discharged 257 days after birth.

Discussion

Recently, a decrease in the number of obstetricians has been a serious social issue in Japan. As a result, patients with obstetric complications, including acute appendicitis, are usually taken to a hospital with a high-volume perinatal center, such as our institute, after being transferred from surrounding hospitals including rural hospitals since obstetricians were not working in these hospitals. Especially, collaboration between general surgeons and obstetricians is required for immediate treatment of acute appendicitis in pregnant patients. Although acute appendicitis is the most frequent disease in the acute abdomen during pregnancy

Table 2 Comparison of the clinical characteristics between the preterm labor and non-preterm labor groups

| | Preterm labor (<i>n</i> = 10) | Non-preterm labor (<i>n</i> = 23) | <i>P</i> value |
|--------------------------------------|--------------------------------|------------------------------------|-----------------|
| Preoperative WBC (mm ³)* | 14,850 | 14,200 | 0.33 |
| Preoperative CRP (mg/dl)* | 12.7 (0.1–21.5) | 1.95 (0.1–19.5) | 0.003 |
| Time to operation (h)* | 24 (3–72) | 24 (5–72) | 0.16 |
| Types of anesthesia | | | 0.03 |
| General anesthesia | 5 (50 %) | 2 (8.7 %) | |
| Lumbar anesthesia | 5 (50 %) | 21 (91.3 %) | |
| Incision method | | | 0.12 |
| McBurney | 2 (20 %) | 13 (56.5 %) | McBurney:others |
| Pararectus | 7 (70 %) | 9 (39.1 %) | |
| Median | 0 (0 %) | 1 (4.4 %) | |
| Transverse | 1 (10 %) | 0 (0 %) | |
| Operative time (min)* | 68 (20–100) | 53 (33–120) | 0.57 |
| Pathology of the resected appendix | | | 0.02 |
| Catarrhalis | 0 (0 %) | 8 (34.8 %) | |
| Phlegmonous | 3 (30 %) | 8 (34.8 %) | |
| Gangrenous | 7 (70 %) | 7 (30.4 %) | |
| Duration of antibiotic use (days)* | 2 (1–10) | 3 (0–6) | 0.1 |
| Surgical site infection | 0 (0 %) | 2 (8.7 %) | 0.87 |

* The data indicate the medians and ranges

[1], little is known about the actual management of acute appendicitis during pregnancy under such medical conditions. Previous studies [2–5] have reported an occurrence of acute appendicitis during pregnancy of one in every 1500 pregnant females, representing an overall incidence of 0.06 %. Among the 13,479 deliveries performed during our study duration, the incidence of acute appendicitis was 1/408 (0.24 %), which was extremely high compared with previous reports [2–5]. Furthermore, the pregnant patients with acute appendicitis accounted for 9.1 % (33/361 cases) of the females with acute appendicitis. As we mentioned above, pregnant patients with acute appendicitis from the surrounding area were treated at our institute, which has a high-volume perinatal center. Of the pregnant patients with acute appendicitis, the incidences of those in their first and second trimester were almost the same, while the incidence of those in their third trimester was relatively low at 6.1 %. Previous reports [2, 6] demonstrated that the frequency of second trimester cases was slightly predominant. However, there is no consensus concerning this point. Andersson et al. [7] suggested that pregnancy reduces the incidence of acute appendicitis, especially during the third trimester. They hypothesized that during pregnancy the immune system experiences a shift towards a T-helper cell type 2 (TH2)-dominant immunity with depressed cellular inflammatory responses and increased humoral immunity during pregnancy, while a decrease in T-helper cell type 1 (TH1)-mediated chronic inflammation is observed. Appendicitis is an inflammatory process, and the inverse relationship

between appendicitis and pregnancy may suggest that the inflammatory response in appendicitis is mediated by TH1 cells. Therefore, pregnancy protects against appendicitis, especially during the third trimester, and this phenomenon may make it easier to understanding our data.

Regarding the diagnosis of acute appendicitis, it has been reported that physiological and hematological examinations are not always useful, since pregnancy status can interfere with those results. It is believed that anatomical changes in the location of the appendix during pregnancy influence the localization of abdominal pain [8, 9]. Other clinicians have demonstrated that pain in the right lower quadrant of the abdomen is the most common presenting symptom regardless of gestational age [2, 5]. In our study, this was the most frequent symptom throughout each trimester. Moreover, the preoperative WBC count in the PG was significantly higher than that in the CG, while the CRP level was not significantly different between the two groups. The difference in elevated WBC counts might be explained by the difference in the baseline counts of pregnant versus non-pregnant females. We analyzed the postoperative WBC count (4 or 7 days) in the PG and CG. The median WBC count was 7150 in the PG and 5900 in the CG. There was statistical significance in the postoperative WBC between the PG and CG ($P < 0.001$). However, we speculated that few healthy pregnant females have WBC counts greater than 10,000. Therefore, an elevated preoperative WBC count exceeding 10,000, together with other clinical findings, could support the diagnosis.

The use of radiological resources in pregnant females to examine the appendix is still controversial, while there is no argument regarding the use of US primarily for the diagnosis of acute appendicitis. Previous reports [10, 11] have suggested that US is a useful modality to observe the appendix. Most reports have shown a diagnostic yield of acute appendicitis up to 70 %. By contrast, because the diagnostic capability depends on technical skills, there have been some negative views regarding the usefulness of US [3, 12]. In our series, 24 patients (72.7 %) were diagnosed with acute appendicitis using US, while nine patients (27.3 %) failed to show preoperative findings in the appendix. As a consequence, those patients underwent CT examination, resulting in a diagnosis of acute appendicitis. Freeland et al. [12] demonstrated that CT or magnetic resonance imaging (MRI) is recommended as an additional examination if US fails to be diagnostic in pregnant patients. In general, the gestational duration of 10–17 weeks might be a high risk for radiation-induced teratogenesis, and the cumulative exposure of more than 50 mGy could exert a deleterious effect on the fetus [13]. Angel et al. [14] reported that the average dose of a single abdominal-pelvic CT exposure was 10.8 mGy. Castro et al. [15] suggested that the use of selective limited helical scanning reduced radiation exposure to 3 mGy. MRI has been advocated as a useful modality instead of CT examination [16]. However, little is known about the long-term influence of gadolinium chelates and electromagnetic disturbance on the fetus. Taken together, we would like to emphasize that CT examination should be performed without hesitation in pregnant patients considered to receive any benefit from such diagnostic investigations.

Surgical procedures may increase the risk of poor pregnancy outcomes. In the present study, no significant differences were found between the PG and CG in terms of the type of anesthesia, operative method, operative time, pathology of the resected appendix, duration of antibiotic use, and incidence of wound infection. Of the 33 cases evaluated, lumbar anesthesia was performed in 26 (first trimester, 13 cases; second trimester, 13 cases). Two patients in their third trimester underwent general anesthesia. Previous reports [17, 18] suggest that no specific type of anesthesia or surgery is associated with an increased incidence of adverse reproductive outcomes. Therefore, the type of anesthesia may not be associated with risk in the patient or fetus regardless of the gestational age. Regarding the incision method, pararectal incision accounted for approximately 50 % of the cases in the PG, while McBurney's incision was performed in up to 75 % of the CG patients. Transverse incision has been reported as a major approach for appendectomy in pregnant patients [8, 19]. The incision over McBurney's point appears to be sufficient for treatment of appendicitis during pregnancy regardless

of the incision method or gestational age [8]. We prefer pararectal incision to transverse incision, because it might stimulate the uterus less. Imaging examinations, including US and CT, will serve as useful methods for determination of the incision method used. Although all of the patients underwent open appendectomy in our study, many reports [20–22] have shown that laparoscopic appendectomy during pregnancy is an effective, feasible, and safe approach in terms of a shorter hospital stay, fewer postoperative complications such as wound infection, abortions, or preterm delivery, and cosmetic problems. However, these reports compared a small number of patients who underwent laparoscopic appendectomy. A recent meta-analysis comparing laparoscopic and open appendectomies demonstrated that laparoscopic appendectomy performed during pregnancy might be associated with a greater risk of fatality [23, 24]. This point needs to be addressed in the era of laparoscopic surgery. Regarding conservative treatments of appendicitis, antibiotic therapy could be an alternative to appendectomy, although the adequacy of antibiotic therapy for treatment of pregnant appendicitis is still unknown. Recent reports [25–28] suggest that appendectomy is still the gold standard therapy for acute appendicitis. Decisions will be made with the safety of the pregnant patients as the highest priority. Therefore, we perform appendectomy as the first-line treatment for pregnant patients with appendicitis.

With regard to the surgical procedure, tocolytic agents are used in patients either prophylactically or following the development of postoperative uterine contractions. In our study, tocolytic agents were used in most of the patients, especially those in their second and third trimesters, after consultation with obstetricians. In fact, 10 patients revealed symptoms of preterm labor, of which one patient (3 %) underwent preterm delivery during the second trimester. However, a recent review revealed no statistical difference in the rate of preterm delivery between the prophylactic tocolysis and the non-tocolysis groups [23]. Therefore, the use of prophylactic tocolytic agents is not considered necessary but can be appropriate if obstetric criteria, such as uterine contractions and the risk of premature birth, exist. In these cases, surgeons should work in close cooperation with obstetricians in clinical practice. Among the pregnant patients with acute appendicitis, a higher preoperative CRP and more severe histological type were associated with the symptoms of preterm labor. Severe inflammation potentially influences the outcomes of preterm labor.

In conclusion, we successfully managed a case of acute appendicitis during pregnancy without fetal loss. In addition to the physiological and hematological findings, US and CT are considered to be useful modalities to reach a definite diagnosis, as long as clinicians understand its safety and efficacy. Moreover, it is necessary to treat the

uterus carefully during surgery regardless of the operative method to prevent preterm labor and abortion.

Conflict of interest Drs. Kumamoto, Imaizumi, Hokama, Ishiguro, Ishibashi, Baba, Seki and Ishida have no conflicts of interest or financial ties to disclose.

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