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Pregnancy Outcomes and Surgical Management of Pregnancy Complicated By Appendicitis: Obstetrician View

Apandisit ile Komplike Gebeliklerin Cerrahi Tedavisi ve Gebelik Sonuçları: Obstetrisyen Görüşü

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Abstract

Objective: To evaluate the pregnancy outcomes of patients who underwent appendectomy during pregnancy.

Materials and Methods: Patients who underwent appendectomy between years 2010 and 2014 were retrospectively evaluated. All patients' pregnancy outcomes were followed-up by using university registry system and telephone interview. Patients were evaluated regarding age, gestational age, clinical and laboratory examinations, imaging studies, mean time interval between emergency department and operation, mean operative time, pregnancy outcome and pathologic results of the appendix.

Results: Thirty-nine patients were included in the study. Sixteen of 39 patients were in the first, 15 of them in the second and 8 of them were in the third trimester of the pregnancy. Three patients underwent laparoscopic appendectomy and the rest underwent laparotomy. In pathologic evaluation of the appendix, seven patients (17%) had normal appendix, 4 patients had perforated appendix, one patient had neuro-endocrine tumor and rest of the patients had appendicitis. Two missed abortion occurred after operation, rest of the patients had live birth. Six of them were preterm and 31 had term birth. Twelve patients delivered through vaginal birth and the rest via caesarean section. Twenty patients were in the first half of the pregnancy (group 1) and 19 patients were in the second half of the pregnancy (group 2). There were no significant differences between the groups in operation time and mean time interval between emergency administration and operation.

Conclusion: Delayed operation and negative appendectomy can cause adverse pregnancy outcomes. Expectant management in suspected cases may decrease negative appendectomy rates but can also lead to perforation. Computed tomography and MRI ought to be considered if ultrasonography is inconclusive. Tocolytic regimens can be administered to prevent threatened preterm labor. Obstetric indications were valid for delivery mode.

Özet

Amaç: Gebeliğinde apendektomi yapılan hastaların gebelik sonuçlarının değerlendirilmesi.

Gereç ve Yöntemler: 2010-2014 yılları arasında apendektomi yapılan hastalar retrospektif olarak incelendi. Tüm hastaların gebelik sonuçları üniversite kayıt

Key words
Appendicitis, pregnancy, surgical management

Anahtar kelimeler
Apandisit, gebelik, cerrahi tedavi

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sistemi ve telefon görüşmeleri ile takip edildi. Hastalar yaş, gebelik yaşı, klinik ve laboratuvar muayeneleri, görüntüleme çalışmaları, acil servis ve operasyon arasındaki ortalama zaman, ortalama operasyon süresi, gebelik sonucu ve apandiksin patoloji sonucuna göre değerlendirildi.

Bulgular: Otuz dokuz hasta çalışmaya dahil edildi. Otuz dokuz hastanın 16'sı ilk, 15'i ikinci ve 8'i gebeliğin üçüncü trimesterindeydi. Üç hastaya laparoskopik apendektomi kalanlarına laparatomi yapıldı. Apendiksin patolojik değerlendirilmesinde, yedi hasta (17%) normal apendiks, dört hasta perfore apendiks, bir hasta nöro-endokrin tümor ve kalanları apandisit saptandı. Operasyon sonrası iki missed abortus meydana gelirken kalanları canlı doğum yaptı. Bunlardan altısı preterm ve otuz biri term doğum yaptı. On iki hasta vajinal yolla ve kalanları sezaryen yoluyla doğurtuldu. Yirmi hasta gebeliğin birinci yarısında (grup 1) ve 19 hasta gebeliğin ikinci yarısındaydı (grup 2). Gruplar arasında operasyon zamanı ve acile kabul ile operasyon arasındaki ortalama zaman aralığı açısıdan anlamlı farklılık yoktu.

Sonuç: Gecikmiş operasyon ve negatif apendektomi olumsuz gebelik sonuçlarına neden olabilir. Şüpheli olgulardaki izlem tedavisi negatif apendektomi oranlarını düşürebilir; ancak aynı zamanda perforasyona neden olabilir. Bilgisayarlı tomografi ve manyetik rezonans görüntüleme, ultrasonografinin net olmadığı zaman düşünülmelidir. Erken doğum tehditini önlemek için tokolitik rejimler uygulanabilir. Doğum şekli için obstetrik endikasyonlar geçerlidir.

Introduction

Pregnancy is the period of life in which most of the pathologic symptoms may be supposed as physiologic changes. Hormonal changes cause nausea, vomiting, heartburn, gastro-esophageal reflux, and urethral dilatation in pregnancy. Enlarged uterus affects localization of the pain. Thus, pregnant patients with suspected appendicitis present a diagnostic dilemma (1). Appendicitis is the most common reason for non-obstetrical surgical intervention in pregnancy. However, it is a rare event with reported incidence to be between 1:1250 and 1:1500 pregnancies (2,3). In a population-based study involving 7 million pregnant patients, the incidence was reported to be 1/1000 (4). In spite of its frequency, an accurate diagnostic method or clinical finding is missing. Ultrasound, magnetic resonance imaging (MRI) and computed tomography (CT) could be performed for diagnosis but these techniques have different specificity and sensitivity rates.

Delayed operation has been thought to be associated with a higher risk of perforation, fetal mortality, and postoperative morbidity (5-7) since Babler first reported these complications 100 years ago (8). However, this approach has caused a higher negative appendectomy (NA) rates in pregnancy (7,9). A high NA rate, therefore, has been accepted in pregnancy and justified in an attempt to avoid perforation and its presumed complications (8); it is apparent that NA is not as innocent as it is supposed. In a study, 30% of pregnant women who sustained a fetal loss or early delivery after operation had a NA (10).

The purpose of this study was to evaluate the pregnancy outcomes of patients who underwent appendectomy with obstetrician view.

Materials and Methods

Pregnant patients who underwent appendectomy between January 2010 and December 2014 in Ege University, Faculty of Medicine were retrospectively reviewed. Patient data on emergency department/operating room admissions were analyzed. Clinical presentation, gestation period, physical examination, Alvarado score, diagnostic modalities, laboratory findings, operation findings, pathological results, tocolysis requirement and post-operative complications were evaluated. Gestational age was calculated from the first day of the mother's last menstrual period or by ultrasound measurements. Abdominal ultrasound imaging was performed by radiology physicians in the emergency department. All patients' pregnancy outcomes were followed-up by using university registry system and telephone interview.

The patients were subdivided into two groups depending on pregnancy weeks. The first group included patients at less than 20 weeks' gestation and the second group consisted of patients beyond 20 weeks' gestation. Time elapsed between emergency admission and operation and time of operation were compared between the two groups.

Statistical Analysis

Statistical analysis was performed using the SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) software for Windows. Statistical analysis included differences between the groups and Fisher's exact and the Mann Whitney tests were used for analyzes. A p-value of less than 0.05 was considered statistically significant.

Results

Thirty-nine patients underwent appendectomy in our hospital. The mean age of the patients was 31±6.3 years. The median gestational age at the time of operation was 19 weeks. All patients were admitted to the emergency department with abdominal pain. The patients were subdivided into two groups according to gestational age. Group 1 involved 20 patients who were in the first half of the pregnancy; group 2 included 19 patients in the second half of the pregnancy.

The demographic properties, clinical findings, laboratory findings and pathologic results are summarized in Table 1.

The median time interval between pain onset and emergency admission was 1 day (range: 4 hours-7 days). The mean time interval in all patients from emergency room admission to operation was 845 minutes. This time interval was 849 minutes (range: 70-1450 minutes) in group 1 and 649 minutes (range: 130-1380 minutes) in group 2. The difference was not statistically significant (p=0.227). These two groups were compared for operation time which was 56 and 60 minutes, respectively; there was no statistically significant difference (p=0.191).

Ultrasound was the first imaging technique. All the patients were evaluated by ultrasound. If ultrasound was inconclusive or was not able to visualize, CT was offered. Yet, none of the patients accepted it. Ultrasound reports and results of pathological investigation are shown in Table 2. Pregnancy data, outcomes and complications are summarized in Table 3.

Two patients had missed abortion after operation. Pathologic results of these two patients were normal appendix. Two wound infections had occurred. One of these patients had preterm birth; the other patient had birth at term.

One patient, who was 30 weeks pregnant, was admitted to the emergency department with abdominal pain and vaginal bleeding on post-operative 8th day; emergency caesarean section was performed, and abruption placenta and abdominal abscess was exposed.

One patient was re-operated because of internal herniation and evisceration on post-operative 6th day. This patient had term birth via caesarean section.

Negative appendectomy was performed in 7 patients. Six of 7 patients were in the first trimester of the pregnancy. All the patients had nausea and vomiting. Five of them had positive peritoneal sign. Four of them had positive C-reactive protein levels and fever. Ultrasound performed in all patients. Appendix was not able to be visualized in five patients

Table 1. Patients' demographic, clinical, laboratory and pathologic findings

	Patients <20 gestational week	Patients >20 gestational age
Mean age	29.8±5.2	31.5±6.3
Fever >38.5 ^{0}C	4	10
Abdominal tenderness	20	19
Pain Localization	5 generalized 12 right lower quadrant 3 right upper quadrant	4 generalized 13 right lower quadrant 2 right upper quadrant
Positive peritoneal signs	17	17
Hyperleukocytosis >15.000/mm^3	5	12
Nausea and vomiting	18	15
Alvarado scoring (median)	6	9
C-reactive protein >0.5 mg/dL	16	14
Ultrasound findings	10 Not able to visualized 4 Normal 6 Appendicitis	8 Not able to visualized 2 Normal 9 Appendicitis
Pathologic results	6 Normal 1 Neuroendocrine tumor 2 Perforatedappendicitis 11 Appendicitis	1 Normal 16 Appendicitis 2 Perforated appendicitis

and appendicitis was reported in 2 patients. Two of the patients had missed abortion after the operation and rest of them had term birth.

Discussion

Appendicitis is a true emergency that may cause morbidity and even mortality. Diagnosis in pregnant patients is not easy because of the physiological changes. There is a general reluctance to operate unnecessarily on a gravid patient. On the other hand, it is the fact that delayed operation can lead perforation and complication.

Acute abdominal pain is the major symptom. Localization may differ because of the enlarged uterus. This enlargement can affect the pain localization, mask or delay peritoneal signs. However, in a recent prospective study, the authors compared the localization of appendix in term pregnant patients who underwent elective caesarean section, in pregnant patients who underwent appendectomy and in non-pregnant patients who underwent appendectomy. They showed no significant difference in appendix localization between the three groups (11). Yet, the authors did not give any information whether they checked appendix location before or after birth of child in caesarean section. In our study, 25 of 39 patients (64%) had experienced right lower quadrant pain. We believe that pain location is related with inflammation and location of the appendix.

Ultrasound is the first diagnostic imaging method. In different studies, accuracy of ultrasound for diagnosing appendicitis has been reported between 30% and 98% (12-14). In another study, it is stated that if appendicitis is reported by ultrasound, no further confirmatory test is necessary other than surgery (15). In our study, appendix was not possible to be visualized in 18 patients (46%). In the rest of the patients, ultrasound has detected 15 of 19 patients with a sensitivity of 78%. Appendix was visualized as normal in 4 patients but histopathologic findings of the entire appendectomy specimens revealed appendicitis. The major problem of the ultrasound was dependent on physician and experience.

Computed tomography was offered to patients with suspected appendicitis in our study, but none of the patients had accepted it. The obstetricians and the patients were reluctant to CT. Nevertheless, the exact threshold at which no teratogenic effects occur to the fetus is estimated to be between 0.05 and 0.15 Gy or 5 to 15 rad. The estimated dose of ionizing radiation associated with a CT in a pregnant

Table 2. Ultrasound reports

Usg report	Pathology report appendicitis	Pathologic report normal appendix
Not visualized n=18	13	5
Appendicitis n=17	15	2
Normal n=4	4	0

Table 3. Pregnancy data, outcomes and complications

	Patients <20 gestational age n=20	Patients >20 gestational age n=19
Gestational age in operation time (week)	Mean: 11 Median: 11 Range 5-18	Mean: 28 Median: 26 Range 20-35
Pregnancy outcomes	2 Post-operation abortion 1 preterm labor 17 Term labor	5 preterm labor 14 Term labor
Occurred preterm threatened labor	1	3
Mode of delivery	9 Vaginally 9 Caesarean section	3 Vaginally 16 Caesarean section
Complications	2 Abortion 1 Wound infection	1 Wound infection 1 Abdominal abscess + abruption placenta 1 Evisceration re-operation

patient for appendicitis is between 0.024 Gy (2.4 rad) in the first trimester and 0.046 Gy (4.6 rad) in the third trimester (16,17). Although there are not many studies investigated the efficacy of CT in pregnant patients, in two studies, the authors have found that CT scan has a negative predictive value of more than 95% in pregnant patients with abdominal pain (18,19). Thus, CT is an alternative imaging method to avoid NA.

MRI is another alternative technique for diagnosis in patients that ultrasound is inconclusive. MRI appears to be preferable even in the first trimester unless gadolinium-based MR contrast agent is not administered (20). Although it is expensive and is not available in all emergency departments, the sensitivity and specificity of MRI for the detection of appendicitis in pregnancy has been reported to be 100% and 93.6%, respectively, in a small series (21).

The surgical technique is dependent on surgeon's experience and skill. In the past, laparotomy was the only approach for appendectomy during pregnancy. As laparoscopic techniques advanced, laparoscopic appendectomies became more common in pregnancy as well (22). The potential advantage of laparoscopic appendectomy over appendectomy is related to the fact that laparoscopic appendectomy is performed via smaller abdominal incisions, associated with lower wound infection and shorter length of hospitalization in the general population (23).

Laparoscopic appendectomy is technically feasible in all trimesters of pregnancy and is associated with the same benefits of laparoscopic surgery. However, some authors propose the 28th week as the upper limit of the gestational age (24). Latest reviews have stated that laparoscopic appendectomy in pregnancy is associated with a greater risk of fetal loss and no significant difference was found for wound infection, birth weight, length of hospital stay, duration of operation and Apgar score (25,26). However, contrary to these articles, there are many studies showing that laparoscopic approach did not influence fetal loss (27-30).

There are some critical points in laparoscopic surgery in pregnant patients. Access to the peritoneal cavity must be based on the size of the uterus. Open Hasson technique, Veres needle or Palmer's point could be used to access into the abdomen. Pneumoperitoneum will decrease venous return, cardiac output, and uteroplacental blood flow. To avoid fetal acidosis, pneumoperitoneum pressure should be limited between 12 and 15 mmHg and careful anesthetic attention should be performed to avoid maternal acidosis (31). In our study, three patients were operated on laparoscopically and no complication had occurred.

Seven of 39 (17%) patients had NA. Previous studies have reported a NA rate of 11% to 50% in pregnancy (32,33). Our rate is consistent with the literature, however, two of these patients had abortion after the operation and one of them had a second operation because of ileus three months later. The rest of the patients had birth at term. Ito et al. compared pregnancy outcomes of the patients in NA, appendicitis and perforated appendicitis groups (34). They found no statistically significant difference between the groups. However, eight patients (25%) had preterm delivery and 1 patient had (3%) missed abortion. In another study, McGory et al. (35) concluded that NA in pregnant women is associated with a significant risk of fetal loss. Thus, NA is not risk-free in pregnant patients. An early exploration could cause fetal adverse outcomes.

Four patients had perforated appendicitis. One of these patients had premature rupture of membrane within two days and delivered via caesarean section. The rest of them delivered at term.

The time interval between emergency department admission to operation and operation time was compared between patients at less than 20 weeks' gestation and over. No statistically significant difference was found between the groups. The mean time interval between admissions to operation was 751 minutes. In NA group, this interval was 845 and was 770 minutes in perforated group. Kapan et al. (36) suggested operating patients within 12 hours and Yilmaz et al. (14) suggested 20 hours but they had many perforated patients in their serial.

The benefit of prophylactic tocolysis has been debated, as many studies have noted no benefit for the prevention of preterm birth (37,38), unless contractions have commenced. We administrated prophylactic progesterone treatment to patients at less than 24 weeks' gestation. If the patients had contraction after operation, tocolytic regimens were used. In a large population-based study, the increase in the rate of preterm birth was statistically significant in patients who had appendectomy and especially in patients with peritonitis (4). Six patients underwent preterm delivery

in our study. These patients delivered at least 30 days after the operation, thus, we considered these births not to be associated with the operation.

Appendectomy in pregnancy is not an indication for caesarean section. In our serial, 25 of 38 patients delivered via caesarean section, however, 13 of these patients were operated because of recurrent caesarean and 5 had obstetric indications. The rest of the patients had not delivered in our hospital. In a recent study, it has been stated that the rate of caesareans was almost doubled in the presence of peritonitis, nevertheless, they were consistent with traditional teaching that promotes caesarean section only for obstetrical indications (4).

In conclusion, appendicitis is a true surgical emergency that requires prompt surgery. Delayed operation and NA can cause adverse pregnancy outcomes. Expectant management in suspected cases may decrease NA rates but can also cause perforation. CT and MRI might be considered if ultrasound is inconclusive. Tocolytic drugs can be administered to prevent threatened preterm labor.

Informed Consent: Consent form was filled out by all participants, Concept: Deniz Şimşek, Design: Deniz Şimşek, Data Collection or Processing: Ahmet Mete Ergenoğlu, Halit Batuhan Demir, Taylan Özgür Sezer, Çağdaş Şahin, Analysis or Interpretation: Deniz Şimşek, Literature Search: Özgür Deniz Turan, Ahmet Mete Ergenoğlu, Writing: Deniz Şimşek, Özgür Deniz Turan, Peer-review: Externally peer-reviewed, Conflict of Interest: No conflict of interest was declared by the authors, Financial Disclosure: The authors declared that this study has received no financial support.

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