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Acute appendicitis in pregnant – review of the literature and our own experience

Ostre zapalenie wyrostka robaczkowego w ciąży – przegląd piśmiennictwa i doświadczenia własne

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INTRODUCTION

Acute appendicitis (appendicitis) is the most common surgical disease in pregnant and is a risk factor for a healthy pregnancy (1). Moreover it causes an important diagnostic problem. The incidence is estimated at between 1 in 1400 to 1 in 1600 pregnancies (2-5). According to the statistics it occurs slightly more often in the second trimester of pregnancy (2-5)

Summary

Introduction. Acute appendicitis in pregnant women is essential clinical problem. Physiologic differences of pregnancy can cause problems in diagnosis and proper treatment.

Material and methods. In period 2004-2013 35 pregnant women were operated on with clinical diagnosis of acute appendicitis. The diagnosis was proven at the time of operation in 29 cases. Causes of remain 6 cases were related to other intra-abdominal pathology.

Results. In group of 29 patients with acute appendicitis mean age was 28.4 years. Appendicitis occurred most often in second trimester of pregnancy. In all cases occurred pain in the lower right quadrant of the abdomen, in 78% nausea and vomiting were observed and in 75% leukocytosis was higher than 11.0 K/uL. 89.7% patients were operated on in first 24 hours after admission to the hospital.

Conclusions. Surgical treatment of acute appendicitis in pregnant women should be taken in first 24 hours after admission to the hospital.

Streszczenie

Wstęp. Ostre zapalenie wyrostka robaczkowego (OZWR) u kobiet w ciąży stanowi istotny problem kliniczny. Odmienności fizjologiczne związane z ciążą mogą być przyczyną opóźnienia w rozpoznaniu i prawidłowym leczeniu.

Materiał i metody. W latach 2004-2013 operowano 35 kobiet w ciąży z podejrzeniem OZWR. Śródoperacyjnie potwierdzono zapalenie wyrostka robaczkowego w 29 przypadkach. W pozostałych 6 przypadkach przyczyny dolegliwości były związane z inną patologią wewnątrzbrzuszną.

Wyniki. W grupie 29 pacjentek z OZWR średni wiek wynosił 28,4 roku. OZWR najczęściej występowało w II trymestrze ciąży. We wszystkich przypadkach stwierdzano ból w prawym dolnym kwadrancie brzucha, w 78% nudności i wymioty, wzrost leukocytozy powyżej 11,0 K/uL w 75% przypadkach 89,7% pacjentek było operowanych w pierwszej dobie od chwili przyjęcia do szpitala.

Wnioski. Leczenie chirurgiczne OZWR w ciąży powinno być wykonane w ciągu pierwszych 24 godzin od przyjęcia do szpitala.

and is most common in patients between 20 and 30 years of age (6).

Diagnosis of appendicitis in pregnancy is associated with many difficulties at the stage of history taking and physical examination. Physiological pregnancy as well as complicated one are associated with many symptoms which are common with appendicitis, such as nausea, vomiting or eating disorders.

Other diagnostic difficulty may be caused by the location of pain. Patognomical location of pain in appendicitis in the right lower quadrant of the abdomen in typical cases during the pregnancy may not be present, because of the uterus enlargement and in turn intestine displacement especially after the fifth month of pregnancy (7-9). However, the pain in the right lower quadrant of the abdomen is reported to be a constant symptom of appendicitis (3, 10). Pain located in the lumbar region and laterally may be associated with appendicitis located behind caecum, but also with urolithiasis or inflammation of the urinary tract. Anatomically, the right side is particularly predisposed to purulent urinary tract infections because the pressure on the right ureter caused by right sided flexure of the uterus and hormone-dependent decrease in motility of the ureters (11). These two phenomena contribute to urine retention and bacteriuria found in the urine analysis (12).

Many patients have no evidence of fever, white blood cell count is also not reliable as in the course of pregnancy it physiologically grows (13).

At the management of a pregnant patient there is a risk associated on one hand with too late diagnosis with the possibility of perforation, on the other hand with appendectomy in the absence of appendicitis (so-called “negative appendectomy”) (13). In the past, principle aggressive approach and fast qualification for surgery were practiced because it was thought that the risk of negative appendectomy is much smaller for the mother and fetus than restraining from the intervention. Thus, in the current literature, the index of negative appendectomies is as high as 50% (8, 9). A careful analysis of the problem shows that 30% of negative appendectomies ended with miscarriage or preterm birth (14).

However, appendicitis in pregnancy – also treated surgically – carries the risk of perinatal complications. Perinatal complications are observed at a level from 10 to 20% of patients. Fortunately mortality in the present time is at a very low level (11, 12, 15-31).

There is no single treatment protocol recommended and followed by all the medical centers. The most important is the conclusion that the delay in diagnosis definitely worsens the prognosis (32). In recent literature reviews (32) complicated appendicitis was significantly more often associated with miscarriage comparing to the appendicitis without perforation (12.1 vs 3.4%, $P = 0.0027$).

For each acute abdominal pain in pregnancy diagnosis should always lead toward confirmation or exclusion of appendicitis (33). It is important to also remember to exclude potentially fatal pathologies associated with pregnancy such as placenta abruption or uterine rupture (34). Diagnosis should be based on accurate history taking, physical examination, laboratory tests (peripheral blood morphology, urinalysis, liver profile: AST, ALT, also amylase, lipase). These studies are not enough to confirm the diagnosis of appendicitis but they may exclude other acute abdominal diseases

(such as: acute pancreatitis, cholestasis of pregnant, urinary tract infection etc.). CRP level is generally above normal, but may remain within the limits (19, 20) – it does not constitute a patognomic parameter for appendicitis (as it does in the case of non-pregnant patients).

Additionally the standard practice is to perform an ultrasound imaging of the abdominal cavity and the fetus. Please note that an ultrasound in such conditions is extremely difficult. Although in some US studies, the sensitivity of abdominal ultrasound in the detection of appendicitis in children and adults was 98% (but usually is at a level of 86%) and a specificity of 81% (35), be aware that this method is very dependent on the person performing the study. In the presence of pregnancy related changes in the anatomical relations in the peritoneal cavity and the uterus itself, it is very difficult to make correct interpretation and appropriate diagnostic evaluation – hence the rate of positive tests is significantly reduced.

In case of a negative ultrasound (even 97% of appendicitis is not visualized) in cases of doubt should be considered an additional tomography (CT) and/or resonance imaging (MRI) of the abdomen (36). MRI (performed without a solution gadolinium) is of sensitivity of 80 to 86% and specificity of 97 to 99% (37). If MRI is not available it is recommended to perform a CT scan of the abdomen and pelvis with the lowest possible dose of radiation – that is less than 5 rad (standard dose of radiation used in the pelvic imaging is 1 to 5 rads, depending on local protocols) (38, 39).

Comparison of the methods for diagnostic imaging in appendicitis (40-43) (tab. 1 and fig. 1).

Complications of appendicitis in pregnancy:

1. typical for appendicitis:

- perforation of the appendix,
- abscess/periappendical infiltration,
- acute peritonitis,
- wound infection,
- systemic septic complications,
- ileus,
- pneumonia;

2. associated with pregnancy:

- premature contractions,
- premature birth,
- low birth weight of the baby,
- intrauterine fetal death (44).

Algorithm for the management of pregnant patients with suspected appendicitis (13) (fig. 2).

Acute appendicitis in pregnancy is an important issue. The more advanced the age of pregnancy, the more difficult is the diagnosis (12, 15) – as a result of the previously mentioned anatomical changes associated with the growing uterus. In a study of Free-land et al. on appendicitis diagnosis in pregnant (13), 15 to 20% of the patients with negative appendectomy had been diagnosed with another cause of discomfort (e.g. ovarian cyst, twisted fallopian tube, peritoneal lymphadenitis, salpingitis).

Table 1. Comparison of the methods for diagnostic imaging in appendicitis: advantages and disadvantages.

Examination	Advantages	Disadvantages	Sensitivity %	Specificity %
Abdominal ultrasound	<ul style="list-style-type: none"> - no exposition for the radiation - no need of contrast - high availability - low cost 	<ul style="list-style-type: none"> - the result depends on the person performing the examination - often unclear results 	100	96
MRI	<ul style="list-style-type: none"> - no exposition for the radiation - comparing to the ultrasound the result is not so dependent from the person performing the examination 	<ul style="list-style-type: none"> - time-consuming - expensive - requires radiologist experienced with interpretation of MRI - less available 	100	93.6
CT	<ul style="list-style-type: none"> - comparing to the ultrasound the result is not so dependent from the person performing the examination - high availability 	<ul style="list-style-type: none"> - exposition of the fetus for the radiation (small dose from 1 to 4 rad) 	92	99

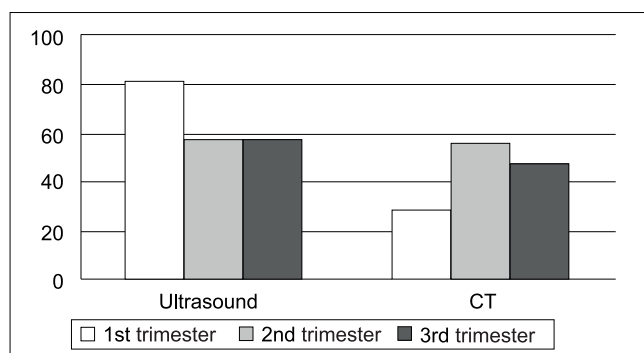


Fig. 1. Comparison of the methods for diagnostic imaging in appendicitis according to the trimester of the pregnancy.

Operation – qualification, selection of access, perioperative management

In the case of suspected appendicitis qualification for surgery should take place within the first 24 hours of observation in order to avoid the risk of perforation or other severe complications (2, 5, 45).

At the time of diagnosis and qualification for the operation, the surgeon is facing with a dilemma: classical surgery or laparoscopic access. The choice of method of operation is the result of many factors and depends on the gestational age, the severity of appendicitis, the

patient’s weight, previous abdominal surgery and the operator’s preference included. In the first trimester of pregnancy classical operation with access via laparotomy, performing McBurney incision in a typical location, which can be extended if necessary, usually ensures an adequate access for appendicitis. In the second and third trimester of pregnancy, it is recommended to open peritoneal cavity a little higher and more towards the right flank. Such access allows surgeon to visualize the pathology of appendix, which at this stage is usually raised together with the caecum by the pregnant uterus (34). When the symptoms of diffuse peritonitis are present, some authors demonstrate the need for median incision which allows quick access to the entire peritoneal cavity (34).

Laparoscopic access is undoubtedly a widely used and accepted in the treatment of appendicitis in non pregnant patients (23). The choice of this type of operation in pregnant patients also still raises a lot of controversy: the risk of injuring the pregnant uterus by trocars, fetal intolerance to high pressure of CO₂ during generation of pneumoperitoneum. Many researches present view that laparoscopic appendectomy is relatively simple to perform, safe, and carries many benefits (38, 46, 47). In one of the studies (48, 49) with 637 laparoscopic appendectomies analyzed, the authors reported a higher

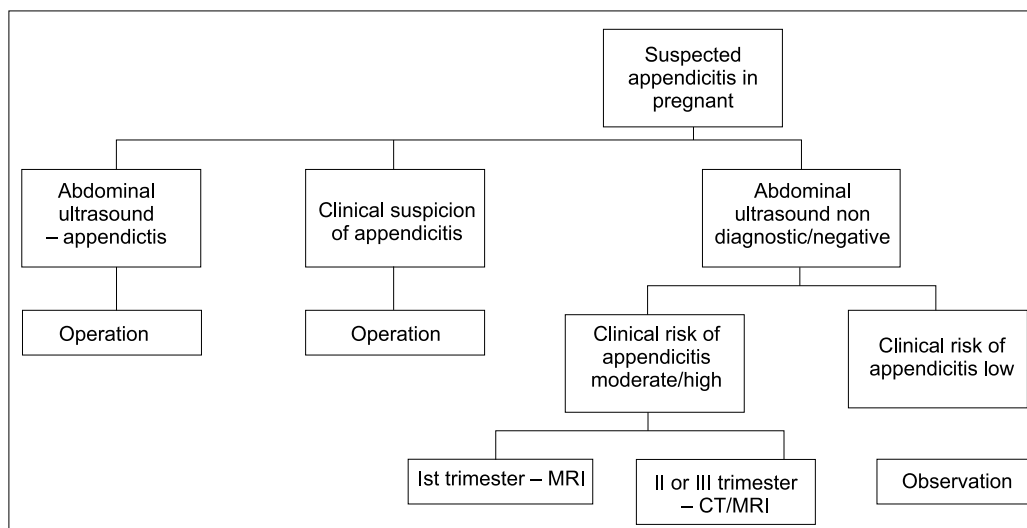


Fig. 2. Algorithm for the management of pregnant patients with suspected appendicitis.

miscarriage rate after laparoscopic vs. open surgery (5.6 vs 3.1%, $P = 0.001$). At the same time the number of preterm births was statistically significantly lower after laparoscopic surgery (2.1 vs 8.1%, $P < 0.0001$). Another research, from Sweden, analyzing 2000 operations of the both accesses in patients between 4 and 20 week of pregnancy showed no statistically significant differences in the prevalence of premature births, low birth weight, fetal malformations or perinatal mortality at 1 year follow-up (50).

The surgical team and anesthetist should be suitably experienced and equipped. In addition anesthetic protocol should be aimed primarily at preventing hypercapnia (47).

Pneumoperitoneum may be generated as with a Verress needle as Hassons method. Trocars positioning should be adequate for gestation age to avoid the uterus injury during the handling/manipulation of the tools. The height of the fundus of the uterus should be assessed by palpation, ultrasound imaging might be also helpful. It is recommended not to exceed 15 mmHg pressure (typically from 10 to 12 mmHg), in some studies 12 mmHg (27, 28). It is important to maintain the pressure at a level as low as possible while maintaining adequate access and visualization of the organs in the peritoneal cavity. It is recommended to position the patient on her left side in decubital position (Trendelenburg) to avoid compression of the vena cava and improve venous outflow. It should be avoided to use the monopolar electrocautery near the uterus (33).

Laparoscopic procedure usually requires the use of three trocars, in the first trimester placed typically (one trocar in the midline over the other two), in the second and third trimester it is recommended to place all three trocars close together and close to the right side of the abdomen, laterally to the right border of the uterus (34). Any manipulation of the uterus should be avoided. If there is a need to move the uterus, the ligament can be grasped (34).

Antithrombotic prophylaxis should include at least the stockings with graduated compression and fast mobilization after surgery. Depending on the risk level of thromboembolic complications, low molecular weight heparins may be indicated (interview concerning diseases in the past, duration of the operation and of the pneumoperitoneum) (51).

In the perioperative period close observation of the patient should be implemented to provide tocolysis if necessary (2). Recommendations for administration of tocolysis are not standardized. Pearl and colleagues believe that there is no need for routine tocolysis in each patient but only in cases of preterm labor starting/premature contractions (52). Other centers use standard tocolysis for each patient (11, 12, 15-31, 34, 53) after 12 weeks of gestation (34).

It is recommended to use analgesics (3) and broad spectral antibiotic therapy (44) to cover the flora of Gram positive, Gram negative and anaerobic (for ex-

ample second-generation cephalosporins, clindamycin, metronidazole) (2, 5).

MATERIAL AND METHODS

We conducted a retrospective study on a group of 35 consecutive pregnant women operated for the suspected acute appendicitis in 2004-2013 at the Department of General, Oncological and Gastrointestinal Surgery of the Hospital Prof. W. Orłowski Centre of Postgraduate Education in Warsaw.

In this group we selected 29 patients with an inflamed appendix revealed intraoperatively. We analyzed the patients' data (age, week of pregnancy), the occurrence of symptoms suggestive of acute appendicitis (pain in the right lower abdomen, a typical pain migration, nausea or vomiting, changes in abdominal ultrasound, indicators of the inflammation: leukocytosis [WBC] and CRP, body temperature and heart rate [HR]) and the results of the histopathological examination. We also obtained the time from the onset of the symptoms to admission, the time from the admission to hospital to surgery, and the time from the surgery to discharge.

RESULTS

In the group of 35 patients operated for suspected acute appendicitis in 29 (83%) an inflamed appendix was found intraoperatively. Histological examination was available in 17 cases (no results in the histories of the disease in 2006 and earlier). The histopathological results were: appendicitis simplex in 4 patients, appendicitis phlegmonosa – 7 patients, appendicitis purulenta – 4 patients, appendicitis stercoralis – 1 patient. In addition, 1 patient with Crohn's disease in the history resulted with changes in the appendix corresponding to Crohn's disease.

In the remaining 6 (17%) patients extra-appendicular pathologies were found: ruptured right ovarian cyst, twisted and ruptured right ovarian cyst, cyst of fallopian tube, torsion of the peri-ovarian cyst, hematic ovarian cyst on the right side and ruptured tubal ectopic pregnancy (the second embryo was present in the uterine cavity).

We further analyzed the group of 29 patients diagnosed with the appendicitis. Patients were at a mean age of 28.4 years (18-37), prevailed patients in the age group of 26-30 years (48%) (fig. 3).

Appendicitis occurred on average at 15.9 weeks of pregnancy (2nd to 38th) before the end of 12th week in 11 patients, between 13th and 24th in 13 patients and after 24th week of pregnancy in 5 patients (fig. 4).

In 2 patients the pregnancy was discovered accidentally during the diagnosis of acute appendicitis. 1 patient with appendicitis was a twin pregnancy.

Patients reported to the Admissions with average 2.7-day duration of symptoms (from 1 to 8 days – the longest in the case of a patient with Crohn's disease). The most common symptoms were pain in the right lower abdomen, which was observed in 100% of patients (29/29) and nausea or vomiting – in 78% of

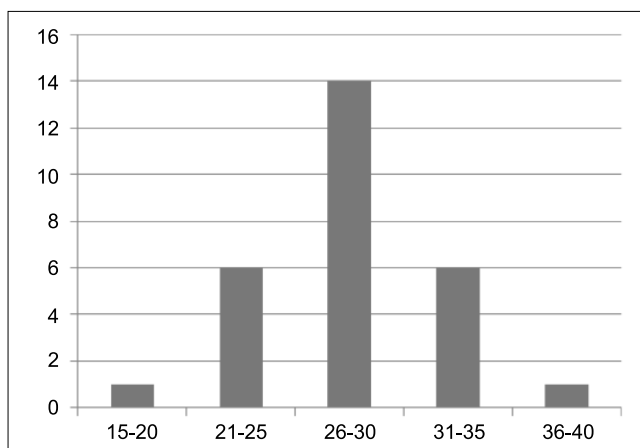


Fig. 3. Number of patients in the age groups.

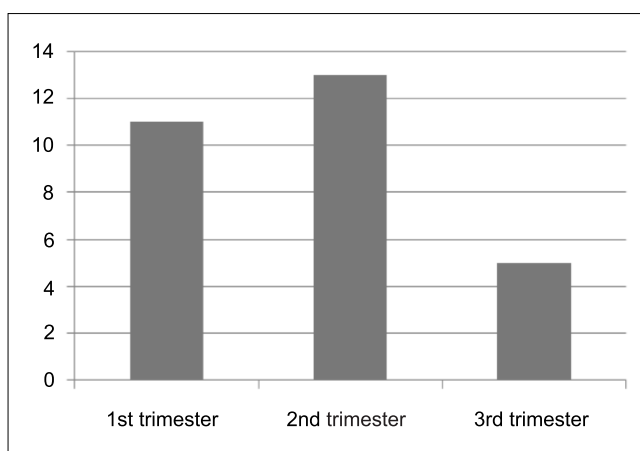


Fig. 4. Number of patients with acute appendicitis divided into trimesters of pregnancy.

patients (21/27). The typical migration of pain from diffuse abdominal pain to the pain localized on the right lower abdomen was observed in 74% of patients (20/27).

The average body temperature at the admission was 36.9 degrees of Celsius (6, 35-37). The temperature equal or exceeding 38 degrees was observed in 2 patients (7%). In the other patients the body temperature remained below 37.5 degrees. Heart rate (HR) was on average 85.7 beats per minute (60-112 bpm). HR of 90 bpm or more was observed in 13 patients, and 100 bpm or more in 7 patients.

The majority of patients had elevated inflammatory parameters: leukocytosis (WBC) and CRP. The mean WBC level was 13.8 K/uL (5.9-22.83 K/uL). WBC exceeded 11.0 K/uL in 22 patients (7%), including 2 cases with WBC exceeding 20 K/uL (7%), and 5 with WBC lower than 10.0 K/uL (17%) which was within the limits for non pregnant. The mean concentration of CRP was 47.6 mg/L (0.8-201 mg/L; measured in 17 patients, no measurements in 2006 and earlier). In 3 patients (18%) CRP did not exceed 10 mg/L (normal). In the remaining 14 patients, serum CRP levels were increased: in 5 patients between 10-30 mg /L, in 3 patients between 30-50 mg /L, in 5 patients between 50-100 mg /L and in 1 patient 201 mg/L.

The result of the abdominal ultrasound was achieved in 25/29 patients. In 19 patients (76%) no pathology

was found, 1 examination was defined “unreliable” due to the gas distension – without visible pathologies, in 2 cases slight and in 1 a significant right ureter distention was found. Symptoms suggestive of acute appendicitis were present in ultrasound in only 2/25 patients (8%): one examination revealed thickened appendix and reactive lymph nodes in the neighborhood, the other, a small amount of fluid in the right side of the abdomen (tab. 2).

Table 2. The incidence of symptoms of acute appendicitis in pregnant.

Symptoms	Prevalence	Percentage
Pain in right lower abdomen	29/29	100%
Typical pain migration	20/27	74%
Nausea/vomiting	21/27	78%
CRP > 10 mg/L	14/17	82%
WBC > 11 K/uL	22/29	76%
Ultrasound – suspected appendicitis	2/25	8%
Body temperature > 38°C	2/29	7%

The majority of patients was operated in the first day of hospitalization: 89.7% (26/29) and in the second day the remaining 3 patients (10.3%). The mean duration of hospitalization after surgery to discharge was 3.0 days (from 2-6 days, we excluded 3 patients, including two transferred to the Department of Gynecology and Obstetrics at day 0. and 2.).

DISCUSSION

Appendicitis in pregnancy is an important diagnostic problem. The patients should be followed by the multidisciplinary care (obstetrician gynecologist, surgeon, anesthesiologist).

The diagnosis is based on a meticulous assessment of the patient, the analysis of additional tests and imaging. Although the high rate of negative results, abdominal ultrasound should be the first imaging study in appendicitis suspicion in pregnant because of its high availability, quick performance, safety for both mother and the fetus, and low cost. If any doubt, do not refuse computed tomography and/or MRI if available. Using MRI still requires further clinical studies involving a larger group of patients.

CONCLUSIONS

The most important conclusion resulting from the review of the literature is the recommendation not to delay a decision on surgery – it should be taken within the first 24 hours of hospitalization. As far as the operating methods are concerned the review of literature is not clear enough which method is better: access via laparotomy or laparoscopy. At the present stage of knowledge, it seems that in the absence of contraindications, a surgeon should select this one at which he feels more confident and that is able to perform quickly and safely.

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