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## Algorithm for acute pancreatitis diagnostics and treatment in pregnant women

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### Abstract

**Introduction.** The problem of early diagnostics and treatment of pregnant women with acute pancreatitis (AP) remains far from being solved despite a significant number of clinical trials [1, 2, 3]. There are still no AP specific recommendations with regard to early diagnostics and treatment. Recently, some sporadic reports on the determination of serum pancreatic elastase levels in pregnant women diagnosed with acute pancreatitis were recorded. At present, there are no available guidelines for the treatment of acute pancreatitis and its complications during pregnancy, emphasizing the role of minimally invasive surgical interventions.

**Objective of the study:** improve the efficiency of acute pancreatitis diagnostics and treatment in pregnant women.

**Materials and methods.** The analysis of diagnostic results and complex treatment of 123 pregnant women was carried out. The treatment group consisted of 61 pregnant women with acute pancreatitis for the period from 2012-2018, using the developed diagnostic and treatment algorithm and the experimental group included 62 pregnant women, from 2006 to 2012, using traditional methods of treatment and diagnosis.

**Results of the study.** According to the results of the study, it can be noted that traditional ways of acute pancreatitis treatment do not take into account the limitations in the use of a number of diagnostic methods in pregnant women, as well as the peculiarities of treatment tactics in different trimesters of pregnancy. Meanwhile, the developed diagnostic and treatment algorithm has significant advantages, i.e.

- early diagnostics based on the determination of elastase 1 at all stages of patient management. It allows detecting acute pancreatitis at an early stage of the disease in 100% of patients in the main group, compared to 48.4% in the comparison group.

- Early use of conservative therapy due to early diagnostics. A positive effect in conservative therapy was achieved in 44.3% of patients in the main group, compared to 33.9% in the comparison group.

- 50.8% of patients in the study group managed to limit themselves to minimally invasive methods of treatment, such as punctures and drainage of fluid formations, endovideoscopic methods of sequestrectomy compared to 46.8% in the comparison group.

- The widespread use of minimally invasive treatment methods allowed to reduce the number of open surgical interventions in the main group up to 4.9% vs. 38.7% in the comparison group, and to avoid mortality vs. 3.2% in the comparison group.

**Conclusion.** The developed diagnostic and therapeutic algorithm for acute pancreatitis in pregnant women in comparison with traditional methods of diagnostics and treatment allows to detect acute pancreatitis at an early stage of the disease. Ensure the effect of conservative therapy in 44.3% versus 33.9%, and to achieve the effect of minimally invasive surgical interventions in 50.8% against 46.8%, open surgical interventions in 4.9% against 38.7% of the comparison group, and to avoid mortality against 3.2% of the comparison group.

**Keywords: pregnancy; acute pancreatitis; diagnosis; treatment.**

**Introduction.** The problem of early diagnostics and treatment of pregnant women with acute pancreatitis (AP) remains far from being solved despite a significant number of clinical trials [1, 2, 3].

Most cases of acute pancreatitis are associated with the presence of cholelithiasis (gallstone disease). Biliary pancreatitis as a complication of gallstone disease is detected in 1,500 - 3,300 pregnant women [5, 6].

The risk of gallstone disease and biliary pancreatitis development increases in case of repeated pregnancy in women with chronic cholecystitis and biliary dysfunction [4, 7].

The acute onset, the nature of the disease and difficulties in diagnostics in the AP treatment pose a significant threat to the health of the mother and fetus [8, 9].

There are still no AP specific recommendations with regard to early diagnostics and treatment. This is largely due to the low incidence rate and pitiful clinical data, as well as the multidisciplinary nature of this condition, when medical care is provided by obstetricians, surgeons, therapists, gastroenterologists, anesthesiologists, etc. [10].

Therefore, AP in pregnant women is often complicated due to the late diagnostics (7-10 days of the disease), as the clinical findings are similar to gestosis in pregnancy, and traditional laboratory diagnostic methods are not always specific at the onset of the disease, as well as due to the inability to use certain instrumental diagnostic methods, such as computed tomography, due to its limited use during pregnancy.

Recently, some sporadic reports on the determination of serum pancreatic elastase levels in pregnant women diagnosed with acute pancreatitis were recorded. It was found under the results of the reports that the pancreatic elastase level is most specific for AP, as it increases in the first 4-6 hours of the disease [8]. A comparative assessment of amylase, lipase, and pancreatic elastase in pregnant women is not performed traditionally.

At present, there are no available guidelines for the treatment of acute pancreatitis and its complications during pregnancy, emphasizing the role of minimally invasive surgical interventions, due to low incidence rates and scant clinical data.

As a result, the diagnosis and treatment of acute pancreatitis in pregnant women is based only on the clinician's experience, which often leads to untimely diagnosis and complications. Therefore, it is advisable to improve the efficiency of early AP diagnostics and treatment in pregnant women.

**Objective of the study:** improve the efficiency of acute pancreatitis diagnostics and treatment in pregnant women.

**Materials and methods.** The paper presents an analysis of the diagnostics and treatment results of 123 pregnant women with AP for the period from 2006 to 2018 at the clinic of the Department of Surgery and Proctology in the P. L. Shupyk National Healthcare University of Ukraine and Kyiv Regional Center of Mothers' and Children's Health Protection.

The patients' age ranged from 18 to 42 years, with a mean age of  $(28 \pm 2.1)$  years. Gestational age ranged from 12 to 37 weeks.

The AP severity in pregnant women was determined under the Atlanta-92 international classification, third revision (2012) [11].

61 pregnant women were included in the main group from November 2012 to April 2018. Acute pancreatitis in the first trimester was found in 18 (29.5%) pregnant women, in the second trimester - 17 (27.9%), in the third trimester - 26 (42.6%) patients. Acute pancreatitis was diagnosed with repeated pregnancy in 21 (34.4%) patients. A history of gallstone disease was observed in 11 (18.0%) pregnant women.

The main group was diagnosed and treated under the improved diagnostic and treatment algorithm.

The comparison group included 62 pregnant women treated from October 2006 to October 2012. AP in the first trimester was found in 17 (27.4%), in the second trimester - in 20 (32.3%), in the third trimester - in 25 (40.3%) patients. AP was diagnosed in 19 (30.7%) patients with repeated pregnancy. There was a history of gallstone disease in 9 (14.5%) pregnant women. Diagnostics and treatment of the comparison group were traditional.

The improved diagnostic and therapeutic algorithm included: besides the study of the anamnesis, assessments of the clinical findings, determination of traditional biochemical parameters of amylase and lipase, determination of pancreatic elastase in the blood serum, as well as a comparative assessment of these parameters on Days 1, 3 and 5 of the disease. A clinical assessment of the disease severity was established based on these data.

Conservative measures were limited to creation of functional rest for the pancreas, pain relief, infusion, antispasmodic, and antienzyme therapy in mild pancreatitis. Monitoring of biochemical blood tests, including serum pancreatic elastase (E1), as well as ultrasound on Days 1, 3, and 5 from the disease onset and at the time of discharge. Magnetic Resonance Cholangiopancreatography (MRCP) was used to establish choledocholithiasis. Endoscopic Retrograde Cholangiopancreatography (ERCP), papillosphincterotomy and lithoextraction were performed if the latter was found. Laparoscopic cholecystectomy was preferred in case of gallstone disease.

Conservative therapy, oxygenation, enteral nutrition, and extended antibiotic therapy were continued in severe pancreatitis. Laboratory parameters were monitored daily, ultrasound, MRI were performed every 3 days. Punctures and drainage under ultrasound control were used in case of increase in size, decrease in echogenicity, edema, accumulation of fluid in the omental sac, parapancreatic spaces more than 50 cm<sup>3</sup>. Laparoscopic removal and drainage of the abdominal cavity was preferred in case of drainage ineffectiveness, in the presence of MRI sequesters.

If any infected necrosis, parapancreatic complications, retroperitoneal phlegmon appeared, open surgical procedures were performed with removal of sequesters and

necrectomy, abdominization of the pancreas, formation of a bursostomy and drainage of parapancreatic retroperitoneal tissue after a primary cesarean section with uterine extirpation.

The AP diagnostics and treatment results, the occurrence of complications in patients of the main and comparison groups were assessed by comparison.

**Results of the study.** 31 (50.8%) pregnant women had abdominal pain and nausea on admission. They had leukocytosis up to  $15.1 \times 10^9 /L$ , unchanged blood amylase and lipase during laboratory control, no changes in the pancreas on ultrasound in the early period. The acute pancreatitis diagnostics was confirmed by the results of serum elastase level that was increased three times up to 10.6 ng/mL, so specific treatment was started.

Leukocytosis up to  $15.1 \times 10^9 /L$  and typical AP complaints were observed in 30 (49.2%) pregnant women from the main group but not all had elevated amylase and lipase levels on admission, only 15 (24.6%) had elevated amylase up to 148.3 units/l, and 18 (29.5%) had lipase up to 239.5 units/l, with characteristic changes in the pancreas. Blood amylase and lipase levels were normal in 12 (19.7%) patients with pancreatitis but the pancreatic elastase level in the serum was tripled up to 11.3 ng/mL.

The diagnosis was confirmed by blood amylase and lipase monitoring on Days 3 and 5, where a gradual increase in their levels as well as changes in the pancreas on ultrasound were recorded. Ultrasound diagnostics found jaundice and choledochal dilation up to 8-10 mm in 13 (21.3%) patients. Magnetic Resonance Cholangiopancreatography (MRCP) was performed. It confirmed the presence of minicholedocholithiasis in 4 (6.6%) pregnant women in the II and III pregnancy trimesters. Endoscopic Fibrogastroduodenoscopy (EFGDS) in patients of the main group showed erosive gastropathy in 37 (60.7%) pregnant women.

Patients were treated under the developed diagnostic and therapeutic algorithm.

Conservative therapy included a number of such measures as reduction of pancreatic secretion, elimination of pain syndrome, enzyme replacement therapy in case of pancreatic exocrine insufficiency development. Infusions of crystalloid and colloidal solutions were used during the first 12-24 hours to correct hypovolemic and water-electrolyte disorders, improve microcirculation and inhibit free radical oxidation. Antispasmodic and non-steroidal anti-inflammatory drugs were also used. Antisecretory drugs, H<sub>2</sub>-blockers, proton pump inhibitors, and opioid receptor agonists were used to reduce pancreatic secretion.

Additional measures were taken in cases of deterioration, including the administration of antibacterial drugs such as cefoperazone or carbapenems if there was advanced pancreatic necrosis. Antispasmodics, magnesium products, micronized progesterone, and prophylaxis of

respiratory distress syndrome (RDS) with betamethasone were used under the standard regimen if there was a threat of pregnancy termination or preterm delivery.

It is important to note that the acute pancreatitis treatment during pregnancy was adequate to the disease severity, taking into account the possible risks to the mother and fetus. The decision on treatment and the choice of optimal therapy was made under the supervision of a team of specialists (surgeon, gynecologist, intensive care physician, gastroenterologist).

27 (44.3%) pregnant women in the main group showed a positive effect of conservative therapy as a result of treatment with the use of the developed diagnostic and therapeutic algorithm. Laparoscopic cholecystectomy was performed in 19 (31.1%) pregnant women with biliary pancreatitis on the background of cholecystitis, after the acute pancreatitis symptoms were reduced, and the general condition was stabilized.

ERCP, papillosphincterotomy with lithoextraction were performed in 4 (6.6%) cases of minicholedocholithiasis followed by laparoscopic cholecystectomy in the second and third pregnancy trimesters.

Conservative therapy was continued with monitoring of laboratory parameters and ultrasound control in patients with an increase in the pancreas size, decreased echogenicity, edema, fluid accumulation in the bursa omentalis, parapancreatic spaces, and fluid accumulation up to 50 mL<sup>3</sup> found with the help of ultrasound. And punctures and drainage of the omental sac were performed under ultrasound control in cases of fluid accumulation of more than 50 mL<sup>3</sup>, and no effect of conservative therapy within 3 days. This method was used in 8 (13.1%) pregnant women in the second and third pregnancy trimesters. Of these, repeated punctures were performed in case of repeated fluid accumulation in 3 (4.9%) cases.

The presence of sequestrers was found during MRI examination in 4 (6.6%) cases. Pregnant women underwent laparoscopic removal of sequestrers and drainage of the abdominal cavity in the second and third pregnancy trimesters.

Open surgical intervention was performed in 3 (4.9%) pregnant women due to complications at Weeks 32, 37, and 38 of pregnancy. During the operations, sequestrers were removed, necrectomy, gland abdominization, bursostomy formation and drainage of parapancreatic retroperitoneal tissue were performed. A hysterectomy without uterine appendages was performed in case of complications. The long postpartum and postoperative periods which lasted  $35 \pm 1.9$  days, ended with a successful recovery of these patients.

The comparison group included 62 pregnant women, of whom 30 (48.4%) had typical complaints and clinical signs of acute pancreatitis, leukocytosis up to  $16.1 \cdot 10^9$  /L, elevated levels of amylase and lipase in the blood up to 349 units /L and 403 units/L, respectively, with

characteristic ultrasound changes. Gallstone disease was found in 12 (19.4%) pregnant women, there were signs of jaundice associated with choledocholithiasis in 2 (3.2%) pregnant women (total bilirubin level up to  $86.2 \pm 1.9 \mu\text{mol/L}$ ).

The remained 32 (51.6%) pregnant women had atypical complaints of acute pancreatitis, which did not allow to exclude gestational toxicosis and leukocytosis up to  $16.2109/\text{L}$ . Blood amylase and lipase levels were within normal limits. The pancreatic elastase level was not measured in the comparison group. It complicated the diagnostics of acute pancreatitis, and the diagnosis was made with a delay of  $8 \pm 2.1$  days compared to the first group.

The gallstone disease without signs of choledocholithiasis and typical Ap-characteristic changes in the pancreas was found in 11 (17.7%) patients with ultrasound examination. However, these patients underwent a repeated ultrasound examination in ( $8 \pm 2.1$ ) days due to the increase in typical complaints and clinical manifestations of AP which found an increase in the pancreas size, blurred contours, increased echogenicity and the presence of omentobursitis. Control measurements of amylase and lipase levels in the blood confirmed a significant increase in these indicators - amylase up to 477.6 units/L and lipase to 543.4 units/L, respectively. An MRI examination made in 3-4 weeks showed the following pathological changes, i.e.:

- The presence of pancreatic necrosis was found in 20 (32.3%) pregnant women
- inflammatory changes in the retroperitoneal tissue associated with the release of pancreatic secretions outside the pancreas in 8 (12.9%) patients
- infiltration of the retroperitoneal tissue was observed without the formation of pancreatic necrosis in one case (1.6%).
- Necrotic pancreatic and parapancreatic fluid accumulations were formed in 12 (19.4%) pregnant women.

The comparison group was treated without the implementation of the developed diagnostic and therapeutic algorithm. Conservative therapy was successful in only 21 (33.9%) pregnant women. This is due to the fact that the diagnosis of acute pancreatitis was made much later compared to the main group, so therapy was started with a delay. Only 15 (24.2%) patients underwent laparoscopic cholecystectomy of the 23 (37.1%) cases of cholecystitis. ERCP with papillosphincterotomy and lithoextraction was performed first, and only then laparoscopic cholecystectomy was performed in 2 (3.2%) cases of choledocholithiasis.

This procedure was not possible IN other pregnant women due to the severity of the disease.

Open surgical interventions were performed in 24 (38.7%) cases, including laparotomy with cesarean section, necrosectomy of the pancreas, drainage of the omental sac, and hysterectomy without uterine appendages was performed in three cases of peritonitis in the setting of acute pancreatitis. This is due to the late diagnosis of acute pancreatitis and the occurrence of complications (excessive fluid accumulation, progression of acute infected pancreatic necrosis complicated by peritonitis).

Maternal mortality occurred at 37 and 38 weeks of pregnancy, against the background of septic complications, peritonitis after delivery by cesarean section and hysterectomy. Despite the surgical measures and an expanded range of powerful conservative therapy, it was not possible to improve the course of the disease due to the occurrence of septic complications and multiple organ failure.

Thus, according to the results of the study, it can be noted that traditional ways of acute pancreatitis treatment do not take into account the limitations in the use of a number of diagnostic methods in pregnant women, as well as the peculiarities of treatment tactics in different trimesters of pregnancy. Meanwhile, the developed diagnostic and treatment algorithm has significant advantages, i.e.

- early diagnostics based on the determination of elastase 1 at all stages of patient management. It allows detecting acute pancreatitis at an early stage of the disease in 100% of patients in the main group, compared to 48.4% in the comparison group.

- Early use of conservative therapy due to early diagnostics. A positive effect in conservative therapy was achieved in 44.3% of patients in the main group, compared to 33.9% in the comparison group.

- 50.8% of patients in the study group managed to limit themselves to minimally invasive methods of treatment, such as punctures and drainage of fluid formations, endovideoscopic methods of sequestrectomy compared to 46.8% in the comparison group.

- The widespread use of minimally invasive treatment methods allowed to reduce the number of open surgical interventions in the main group up to 4.9% vs. 38.7% in the comparison group, and to avoid mortality vs. 3.2% in the comparison group.

**Conclusion.** The developed diagnostic and therapeutic algorithm for acute pancreatitis in pregnant women in comparison with traditional methods of diagnostics and treatment allows to detect acute pancreatitis at an early stage of the disease. Ensure the effect of conservative therapy in 44.3% versus 33.9%, and to achieve the effect of minimally invasive surgical interventions in 50.8% against 46.8%, open surgical interventions in 4.9% against 38.7% of the comparison group, and to avoid mortality against 3.2% of the comparison group.



### **Author Contributions**

Conceptualization: Ia. P. F and T. P. P.; methodology: T. P. P.; formal analysis T. P. P.; data curation Ia. P. F and T. P. P.; writing T. P. P.; supervision Ia. P. F. All authors have read and agreed to the published version of the manuscript.

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### **Institutional Review Board Statement**

This case report did not require IRB approval, patient provided verbal and written consent for publication of this report.

### **Informed Consent Statement**

Written informed consent has been obtained from the patient to publish this paper.

### **Data Availability Statement**

All information is publicly available and data regarding this particular patient can be obtained upon request from corresponding senior author.

### **Conflicts of Interest**

The authors declare no conflict of interest.

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