A 23-year, single-center, retrospective analysis of 36 cases of acute pancreatitis in pregnancy

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**A B S T R A C T**

Objective: To assess the incidence, causes, clinical characteristics, and outcomes of cases of acute pancreatitis in pregnancy (aPIP). Methods: A retrospective review was conducted of the medical records of pregnant women who were diagnosed with aPIP at any point during pregnancy, labor, or the puerperium and attended Beijing Chaoyang Hospital, China, between January 1, 1991, and March 31, 2014. Results: Among 34,292 pregnant women admitted to the center during the study period, 36 patients were diagnosed with aPIP. The condition developed during the second [9 (25%) cases] and third (22 [61%]) trimesters. The underlying cause was hypertriglyceridemia for 14 (39%) patients and biliary diseases for 7 (19%). Severe acute pancreatitis was significantly more common among patients with hypertriglyceridemia (11/14 [79%]) than among those without hypertriglyceridemia (6/22 [27%]; \( P = 0.006 \)). Additionally, complications were recorded for more patients with hypertriglyceridemia (31 [79%]) than those without hypertriglyceridemia (4 [18%]; \( P < 0.001 \)). Delayed diagnosis was more common among patients with severe acute pancreatitis (8/17 [47%]) than among those with mild acute pancreatitis (3/19 [16%]; \( P = 0.039 \)). No maternal deaths and only two perinatal deaths were recorded. Conclusion: The overall incidence of aPIP was low; however, hypertriglyceridemia was associated with poor outcomes. Early diagnosis and prompt treatment should be implemented to improve maternal and fetal prognosis and decrease mortality.

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1. Introduction

Acute pancreatitis in pregnancy (aPIP) has a rapid onset and is complicated by rapid progression, frequent misdiagnosis, high mortality, and serious threats to maternal and fetal safety. It is a rare disease, with an incidence of approximately one per 1000–12 000 pregnancies [1–4]. Variation in incidence is attributed to age, diet, alcohol consumption, and genetic variation [5]. Because of its rarity, the number of cases included in most published studies tends to be small.

However, the incidence of aPIP might have increased during the past four decades. The rate recorded in Scotland, UK, increased from 9.4 per 100 000 pregnancies during the period 1968–1980 to 41.9 per 100 000 pregnancies in 1995 [6]. Furthermore, the incidence of aPIP can vary substantially owing to the different incidence of its main causes between ethnic groups, such as gallstones [4]. Few published studies on aPIP have been from China. Given the uncertainty surrounding the incidence, management, and outcomes of aPIP among patients in China, it has been proposed that efforts should be made to conduct studies with large numbers of cases. In addition, prompt diagnosis and suitable treatment of aPIP are essential to ensuring a good prognosis. The aim of the present study was to evaluate the incidence, causes, clinical features, management, and outcomes of all cases of aPIP identified at one center in China during a 23-year period to gain more knowledge of this disease.

2. Materials and methods

A retrospective review was conducted of the medical records of pregnant women who attended Beijing Chaoyang Hospital, Beijing, China, between January 1, 1991, and March 31, 2014. Patients were included in the present analysis if a diagnosis of aPIP had been established at any point during pregnancy, labor, or puerperium. The condition was diagnosed and classified as either mild acute pancreatitis (MAP) or severe acute pancreatitis (SAP) according to the Atlantic Criteria [7]. Diagnosis required at least two of the following clinical features: upper abdominal pain of acute onset, usually radiating to the back; increased levels of serum amylase or lipase (greater than three times the normal levels [172 U/l for amylase and 110 U/l for lipase]); and findings on abdominal imaging consistent with acute pancreatitis. Patients with chronic pancreatitis were excluded. The present study was approved by the institutional review board of Beijing Chaoyang Hospital. Patient records and data were anonymized and de-identified before analysis, so informed consent was not required.

Information was collected from the patients’ medical records regarding maternal age, gestational age at presentation and delivery, potential cause of aPIP, clinical manifestations and complications, diagnostic testing, clinical management, and maternal and fetal outcomes. The data were analyzed using SPSS version 17.0 (SPSS Inc, Chicago, IL, USA). Binary data were presented as number and...
percentage. Demographics were recorded as categorical data. Differences in proportions were compared using the Fisher test. *P* < 0.05 was considered statistically significant.

### 3. Results

During the study period, 34,292 pregnant women were admitted to the study center, and 36 cases of APIP were identified from the medical records. However, seven women had been diagnosed with APIP at affiliated hospitals and were transferred to Beijing Chaoyang Hospital. Consequently, the incidence of APIP at the study center was estimated to be was 29 per 34,285 pregnancies (1 per 1182). Most cases of APIP occurred in either the second (9 [25%] cases) or third (22 [61%]) trimester. The remaining five cases occurred in the first trimester (2 [6%]), during labor (1 [3%]), or in the puerperium (2 [6%]).

The underlying cause of APIP was hypertriglyceridemia (triglyceride level ≥1.13 mmol/L) for 14 (39%) patients and biliary diseases for 7 (19%). Other causes were pre-eclampsia (3 [8%] patients), gestational diabetes mellitus (2 [6%]), gestational impaired glucose tolerance (1 [3%]), hyperemesis gravidarum (1 [3%]), ischemia reperfusion injury (1 [3%]), intravenous infusion of erythromycin (1 [3%]), and labor (1 [3%]). Five (14%) patients had idiopathic APIP.

Among the 14 patients with hypertriglyceridemia, 11 (79%) developed SAP and 3 (21%) developed MAP. Conversely, among the 22 patients without hypertriglyceridemia, 6 (27%) developed SAP and 16 (73%) developed MAP. The observed between-group difference in the incidence of SAP was statistically significant (*P* = 0.006), which suggested that hypertriglyceridemia-induced APIP tended to be associated with a severe clinical manifestation.

The most frequent presentations of APIP were abdominal pain (35 [96%] patients), nausea and vomiting (31 [86%]), and fever (29 [81%]). Other recorded symptoms included anorexia (10 [28%] cases), jaundice (5 [14%]), and diarrhea (2 [6%]). Overall, 15 (88%) of the 17 patients with SAP developed serious complications, including paralytic ileus, pneumonia, electrolyte disturbance, diffused purulent peritonitis, pleural effusion, multiple organ dysfunction syndrome, gastrointestinal bleeding, pseudocyst, pancreatic abscess, and femoral vein thrombosis. Complications were recorded for 11 (79%) of the patients with hypertriglyceridemia, compared with only 4 (18%) of the 22 patients without hypertriglyceridemia (*P* < 0.001).

Elevated white blood cell count, hyperglycemia, severe hypocalcemia, and hypertriglyceridemia were found more frequently among patients with SAP than among those with MAP (*P* < 0.05 for all) (Table 1). Increased amylase and/or trypsinogen-2 activity was detected in the urine of all patients (data not shown).

Transabdominal ultrasonography was performed among 29 (81%) patients; 19 were diagnosed with APIP, four with cholecystolithiasis, one with cholelithiasis, and one with choledochitis. No abnormalities were detected among the remaining four patients, all of whom later underwent computed tomography (CT). Overall, 16 (44%) patients underwent CT; APIP was identified among 15, 11 of whom had SAP and four had MAP.

### Table 1

<table>
<thead>
<tr>
<th>Measure</th>
<th>Severe acute pancreatitis (n = 17)</th>
<th>Mild acute pancreatitis (n = 19)</th>
<th><em>P</em> value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase level &gt;172 U/L</td>
<td>16 (94)</td>
<td>18 (95)</td>
<td>0.513</td>
</tr>
<tr>
<td>White blood cell count &gt;10^9 per L</td>
<td>15 (88)</td>
<td>10 (53)</td>
<td>0.021</td>
</tr>
<tr>
<td>Hyperglycemia*</td>
<td>15 (88)</td>
<td>3 (16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe hypocalcemia*</td>
<td>14 (82)</td>
<td>1 (5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertriglyceridemia*</td>
<td>11 (65)</td>
<td>3 (16)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

* Values given as number (percentage), unless indicated otherwise.

### Table 2

Timing of diagnosis.

<table>
<thead>
<tr>
<th>Timing of diagnosis</th>
<th>Severe acute pancreatitis (n = 17)</th>
<th>Mild acute pancreatitis (n = 19)</th>
<th>Total cohort (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early*</td>
<td>9 (53)</td>
<td>16 (84)</td>
<td>25 (69)</td>
</tr>
<tr>
<td>Delayed*</td>
<td>8 (47)%</td>
<td>3 (16)%</td>
<td>11 (31)</td>
</tr>
</tbody>
</table>

* Values given as number (percentage).

### Table 3

Fetal outcomes.

<table>
<thead>
<tr>
<th>Fetal outcome</th>
<th>First trimester (n = 2)</th>
<th>Second trimester (n = 9)</th>
<th>Third trimester (n = 23)</th>
<th>During labor (n = 1)</th>
<th>Early postpartum period (n = 2)</th>
<th>Total cohort (n = 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal loss</td>
<td>2*</td>
<td>3*</td>
<td>2*</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Premature delivery</td>
<td>0</td>
<td>0</td>
<td>14*</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Term delivery</td>
<td>0</td>
<td>6</td>
<td>7*</td>
<td>1</td>
<td>2</td>
<td>16</td>
</tr>
</tbody>
</table>

* Values given as number.

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* Two patients with severe acute pancreatitis underwent induced abortion.

* Three patients with severe acute pancreatitis underwent induced abortion (n = 2) or had a spontaneous abortion (n = 1).

* One patient had a twin pregnancy (gestational age 28.4 weeks). This patient and her family did not wish to rescue the two fetuses.

* Gestational age 32.0–36.7 weeks; cesarean delivery was performed in all cases.

* Six women developed acute pancreatitis in pregnancy after 37.0 weeks; cesarean delivery was performed for all. The remaining woman developed this condition at 28.4 weeks and received conservative treatments.
Most of the live births (16/30 [53%]) were delivered at term. The remaining 14 live births were premature owing to the need for emergency cesareans. Three (21%) premature neonates were diagnosed with mild asphyxia. One woman developed APIP during labor; she delivered a healthy neonate vaginally and the 1-minute and 5-minute Apgar scores were 9 and 10, respectively. No fetal malformations were observed.

4. Discussion

The present study aimed to gain an understanding of factors influencing APIP in China. The incidence of this condition recorded at Beijing Chaoyang Hospital was one per 1182 pregnancies, a rate in line with previous reports that quote a large range of incidences [1–4]. Diagnosis of APIP was predominantly made during the second and third trimesters, which is consistent with the finding that the frequency of APIP increases as pregnancy progresses [8]. No maternal deaths occurred in the present study and perinatal mortality was low. This observation was in agreement with previous work on maternal and fetal mortalities [3,8,9]. One study credited the decrease in the numbers of maternal and fetal deaths to early diagnosis of APIP and improvements in maternal and neonatal intensive care [9].

Hypertriglyceridemia was the most frequent cause of APIP. During pregnancy, cholesterol and triglyceride levels increase to a different degree because of alterations in hormone concentrations [10]. Hypercholesterolemia alone does not lead to acute pancreatitis in people [11]. However, the risk of this condition increases as plasma triglyceride levels rise to 11.3 mmol/L or higher [12,13]. In the present study, patients whose APIP was undiagnosed by hypertriglyceridemia had an increased tendency to develop SAP and other complications, possibly owing to extensive pathologic changes. The finding that APIP caused by hypertriglyceridemia was associated with poor outcomes is supported by the published literature [3,14,15].

In addition to hypertriglyceridemia, the present study identified biliary diseases and idiopathic factors as key causes of APIP. Other studies have attributed the development of APIP to gallstones (65%–100%), idiopathic causes (15%–17%), alcohol abuse (5%–12%), familial hypertriglyceridemia (5%), and hypertriglyceridemia (4%) [3,16]. Several factors might explain the differences between the present study and the literature. First, the sample size was small owing to the rarity of APIP. Second, the eating habits of patients could vary. Similar to the study of Sun et al. [14], no women reported alcohol consumption in the present study, which might be attributable to concern for the possible adverse effects of alcohol on pregnant women and their fetuses. Third, the incidence of gallstones varies with ethnic origin. For example, indigenous populations in the Americas display a high incidence of gallstones, whereas the incidence reported among Africans and Asians is lower [4]. Furthermore, the ability to metabolize lipids and the genes controlling lipid metabolism might differ by ethnic origin and should be investigated.

Some patients with APIP might not exhibit a specific clinical manifestation owing to the altered location of the pancreas as it is pushed down by the enlarged uterus, and the presence of uterine contractions caused by inflammation. Alterations in blood and biochemical measures that occur as a result of pregnancy could influence the interpretation of diagnostic tests. Furthermore, patients with APIP sometimes develop complications. These factors make it difficult to establish a diagnosis of APIP. Early diagnosis of APIP was not made for 11 of the patients included in the present study. Although measurement of serum amylase and lipase concentrations should be considered during diagnosis, serum levels of lipase are more sensitive and specific than are serum levels of amylase. Unfortunately, serum lipase levels were not measured in most cases in the early phases of the present study (1991–2010) because serum lipase level was not tested if the serum amylase level was higher than 172 U/L.

Transabdominal ultrasonography was the first choice for imaging in the present study, although CT was used in some cases. Transabdominal ultrasonography can provide visualization of the pancreas and some complications (e.g., edema, necrosis, or pseudocysts). Furthermore, this test is safe for pregnant women and costs less than CT. Nevertheless, CT scans can help to diagnose APIP and determine the scale and depth of invasion. This test is also indicated if a patient is experiencing abdominal pain or when ultrasonography fails to detect any lesions. The use of magnetic resonance imaging might also be considered. This technique has not been linked to fetal toxicity and it is an accurate method to identify the cause of acute abdominal and pelvic pain during pregnancy; however, magnetic resonance imaging should be used only when the ultrasonographic findings are indeterminate [17].

Although the present study spanned a period of 23 years, the goal of APIP treatment and the clinical management approach had remained almost the same. Adequate fluid resuscitation is the main goal of initial management. Treatments for APIP are generally conservative and similar to those administered to non-pregnant patients with acute pancreatitis. Exploratory laparotomy should be considered if abdominal pain is not relieved after conservative treatment and a peripancreatic abscess or intra-abdominal abscess is detected.

The underlying causes and complications of APIP should also be treated. Options for hypertriglyceridemia include dietary restriction and lipid lowering. However, the use of lipid-lowering drugs should be restricted to the postnatal period among women with APIP because these agents exhibit slow onset of action and their effects on fetuses are unclear. Plasmapheresis offers an alternative approach to clinical management of severe hypertriglyceridemia should conventional pharmacotherapy fail [18,19]. This method does not appear to have any adverse effects on the mother or fetus [20], although the present study could not confirm safety to the fetus owing to the small number of patients who received this treatment.

Seven patients included in the present study had biliary diseases; exploratory laparotomy and cholecystectomy were performed among two patients with gallstones. One study found that clinicians tended to manage symptomatic biliary tract diseases conservatively during pregnancy [3]; however, Hernandez et al. [2] reported an estimated recurrence rate for biliary pancreatitis of 50% among pregnant patients who had received such treatment. Consequently, severe symptoms such as peritonitis and obstructive jaundice should be considered indicative of the need for cholecystectomy [4]. This procedure can be performed safely throughout pregnancy [21], but might not be offered at advanced gestational ages because of reduced visualization of the pancreas as a result of the enlarged uterus. Endoscopic retrograde cholangiopancreatography is an invaluable diagnostic and therapeutic tool for patients with biliary and pancreatic diseases that has also been demonstrated to be safe during pregnancy [22]. No patients underwent endoscopic retrograde cholangiopancreatography in the present study. Nevertheless, this approach might be considered as an important optional tool for future treatment of APIP at Beijing Chaoyang Hospital.

The findings of the present study suggested that APIP is potentially more dangerous to the fetus than the mother. Timely delivery could improve the maternal condition as well as fetal outcomes. One study noted cesarean delivery as the preferred treatment to prevent further complications [14]. This observation was confirmed in the present study: APIP was cured and the prognosis rates as good among all 21 women who underwent cesarean delivery.

The present study had some limitations. First, patients with APIP were not followed up after the disorder resolved because their records had been anonymized and de-identified, and the contact details provided might have been out of date. Second, owing to the long duration of the present study, some laboratory measurements (e.g., serum lipase level) were not taken for all patients in the early years. Third, there were only 36 cases of APIP in the present study. However, it drew from a large number of cases and so might add valuable practical information to the global knowledge of APIP.

In conclusion, the present Chinese study found APIP to be a rare condition that was most likely to manifest as pregnancy progressed.
often as a result of hypertriglyceridemia. Furthermore, patients with hypertriglyceridemia tended to experience delayed diagnosis and so went on to develop SAP and other complications. Most patients with APIP were cured by conservative treatment. Recognizing the clinical characteristics of APIP, making an early diagnosis, and treating the condition promptly should improve maternal and fetal prognosis.

Conflict of interest

The authors have no conflicts of interest.

References