

Clinical Characteristics and Maternal-Neonatal Outcomes in Acute Pancreatitis of Different Etiologies in Pregnancy: A Postprint

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Abstract

Background: Owing to economic development and changes in domestic fertility policies, the incidence of acute pancreatitis in pregnancy (APIP) has gradually increased. APIP cases with different etiologies exhibit distinct clinical characteristics, and there may be significant differences in maternal and fetal outcomes, which have been rarely studied previously.

Objective: To analyze the clinical features of APIP with different etiologies and their relationship with maternal and fetal outcomes.

Methods: Clinical data of 48 hospitalized APIP patients admitted to Beijing Friendship Hospital, Capital Medical University from 2016 to 2022 were collected. According to etiology, patients were divided into a biliary group (n=27) and a hyperlipidemia group (n=21). Laboratory indicators and maternal-fetal outcomes were analyzed and compared between the two groups.

Results: The time from onset to medical consultation was longer in the biliary group than in the hyperlipidemia group, the gestational age at admission was lower than that in the hyperlipidemia group, the number of previous pregnancies was higher than that in the hyperlipidemia group, and the proportion of diarrhea and cessation of defecation was lower than that in the hyperlipidemia group ($P<0.05$). There was no statistically significant difference in disease severity between the two groups ($P=0.912$). The biliary group had lower levels of hemoglobin, platelets, C-reactive protein, cholesterol, and triglycerides, and higher levels of total bilirubin, direct bilirubin, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, serum creatinine, blood calcium, blood sodium, blood amylase, and N-terminal pro-brain natriuretic peptide than the hyperlipidemia group ($P<0.05$). The gestational age at delivery in the biliary group was shorter than that in the hyperlipidemia group ($P<0.05$). There were no statistically significant differences in the rates

of premature delivery, cesarean section, or artificial intervention to terminate pregnancy via cesarean section between the biliary and hyperlipidemia groups ($P>0.05$). Neonatal weight in the biliary group was lower than that in the hyperlipidemia group, body length was shorter than that in the hyperlipidemia group, and the incidence rates of pathological jaundice, respiratory distress, and ventilator-assisted respiration were higher than those in the hyperlipidemia group ($P<0.05$).

Conclusion: Biliary disease remains the leading cause of APIP, which can significantly shorten gestational age at delivery, cause low birth weight, increase the incidence of pathological jaundice, respiratory distress, and ventilator-assisted respiration, and lead to more severe neonatal outcomes.

Full Text

Analysis of Clinical Characteristics and Maternal and Neonatal Outcomes in Pregnancy Complicated with Acute Pancreatitis Patients of Different Etiologies

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Abstract

Background Due to economic development and changes in domestic fertility policy, the incidence of acute pancreatitis in pregnancy (APIP) has been gradually increasing. The clinical characteristics of APIP vary by etiology, and there may be significant differences in maternal and neonatal prognosis, though previous research on this topic remains limited. **Objective** To analyze the clinical characteristics and maternal and neonatal outcomes in APIP patients of different etiologies. **Methods** We collected clinical data from 48 hospitalized APIP patients at Beijing Friendship Hospital, Capital Medical University from 2016 to 2022, dividing them into a biliary group ($n=27$) and a hyperlipidemic group ($n=21$) based on etiology. Laboratory indicators and maternal-infant outcomes were compared between the two groups. **Results** The biliary group had a longer time from onset to presentation, smaller gestational age at admission, more previous pregnancies, and lower proportions of diarrhea and cessation of defecation compared to the hyperlipidemic group ($P<0.05$). There was no statistically significant difference in disease severity between the two groups ($P=0.912$). The biliary group showed lower levels of hemoglobin, platelets, C-reactive protein, cholesterol, and triacylglycerol, but higher levels of total bilirubin, direct bilirubin, alanine transaminase, alkaline phosphatase, glutamyl transpeptidase, creatinine, calcium, sodium, amylase, and N-terminal pro-brain natriuretic peptide

compared to the hyperlipidemic group ($P < 0.05$). The biliary group also had a shorter gestational age at delivery ($P < 0.05$). No statistically significant differences were observed in premature delivery rate, cesarean section rate, or artificial intervention termination of pregnancy rate between the two groups ($P > 0.05$). Neonates in the biliary group had lower birth weight and shorter birth length, with higher incidences of pathological jaundice, respiratory distress, and ventilator-assisted breathing compared to the hyperlipidemic group ($P < 0.05$). **Conclusion** Biliary disease remains the leading cause of APIP and can significantly shorten maternal gestational age at delivery, cause low fetal birth weight, and increase the incidence of fetal pathological jaundice, respiratory distress, and ventilator-assisted breathing, resulting in more severe fetal outcomes.

Keywords: Acute pancreatitis; pregnancy; acute pancreatitis in pregnancy; maternal-child health services; prognosis

Introduction

Acute pancreatitis in pregnancy (APIP) is a rare but serious condition with acute onset, numerous complications, and high risk of multiple organ failure, posing significant threats to maternal and infant health. Its incidence has been gradually increasing [1]. Although advances in medical care have reduced maternal mortality from 20% to 1% and fetal/neonatal mortality from 50% to 5% [2-3], economic development and changes in domestic fertility policy have led to an increasing number of high-risk pregnant women in China, making APIP a continued serious threat to maternal and infant safety. The main etiologies of APIP are similar to those of acute pancreatitis (AP) in the general population, with biliary tract disease being the most common cause (accounting for over 65% of cases), followed by hyperlipidemia (accounting for 4-30% of cases) [4-5]. However, the clinical features of APIP may differ by etiology, and these differences may significantly impact maternal and neonatal outcomes, though previous research on this topic has been limited. This study collected relevant cases from Beijing Friendship Hospital, Capital Medical University from 2016 to 2022 and analyzed their clinical data to investigate the clinical characteristics and maternal-neonatal outcomes of APIP patients with different etiologies, aiming to provide references for improving clinical diagnosis and treatment of APIP.

The diagnostic criteria and classification for APIP are the same as for AP. According to the 2012 Atlanta and IAP/APA working group diagnostic criteria for AP [6-7], a diagnosis can be established when two of the following three criteria are met: (1) acute onset of persistent severe epigastric pain, often radiating to the back, frequently accompanied by abdominal distension, nausea, and vomiting; (2) serum amylase and/or lipase levels more than three times the upper limit of normal; and (3) abdominal imaging findings consistent with AP. Based

on disease severity, AP is classified into three types: (1) mild acute pancreatitis (MAP) - no organ dysfunction or local complications; (2) moderately severe acute pancreatitis (MSAP) - local or systemic complications without persistent organ failure, or transient organ failure that resolves within 48 hours; and (3) severe acute pancreatitis (SAP) - persistent organ failure lasting more than 48 hours. The diagnostic criteria for biliary acute pancreatitis include meeting the above AP diagnostic criteria while also having gallstones or bile duct stones identified by imaging techniques (such as abdominal ultrasound, MRI, CT, or endoscopic retrograde cholangiopancreatography), or laboratory evidence of abnormal liver enzymes or cholestasis [6]. The diagnostic criteria for hyperlipidemic acute pancreatitis include meeting the above AP diagnostic criteria with concurrent lipemic serum or blood triglyceride levels >11.3 mmol/L [6].

Methods

Study Subjects

We collected and analyzed clinical data from 48 hospitalized APIP patients with biliary or hyperlipidemic etiologies admitted to Beijing Friendship Hospital, Capital Medical University from 2016 to 2022. This study was approved by the Ethics Committee of Beijing Friendship Hospital, Capital Medical University (Approval No.: 2023-P2-129-01).

Research Methods

The 48 eligible APIP patients were divided into a biliary group (n=27) and a hyperlipidemic group (n=21). Basic data, disease severity, laboratory indicators, and maternal-neonatal outcomes were analyzed and compared between the two groups.

Observation Indicators

General indicators included BMI, gestational age at admission, gravidity, Down syndrome screening risk, and time from onset to presentation (days). Clinical manifestations included presence of precipitating factors, fever, nausea/vomiting, abdominal pain, and bowel habits. Laboratory tests included complete blood count, liver function, renal function, serum amylase, blood glucose, blood lipids, electrolytes, B-type natriuretic peptide, D-dimer, C-reactive protein, and procalcitonin. Pregnancy outcomes included gestational age at delivery, delivery mode (artificial termination vs. spontaneous delivery), etc. Fetal outcomes included weight, length, head circumference, Apgar scores (at 1, 5, and 10 minutes), need for hospitalization, presence of pathological jaundice, pneumonia, respiratory distress, need for ventilator-assisted breathing, and mortality.

Statistical Analysis

Data were analyzed using SPSS 26.0 statistical software. Normally distributed continuous variables were expressed as ($\bar{x} \pm s$) and compared between groups using t-tests. Non-normally distributed continuous variables were expressed as M(P25,P75) and compared using Mann-Whitney U tests. Categorical variables were analyzed using χ^2 tests. $P < 0.05$ was considered statistically significant.

Results

General Characteristics

Among 4,890 AP patients hospitalized during the same period, 48 were APIP cases, accounting for 0.98% of all hospitalized AP patients. Among 33,135 pregnant women hospitalized during the same period, APIP accounted for 0.14%. Patient ages ranged from 25 to 39 years, with a mean age of (31.0 ± 4.7) years. There were no statistically significant differences between the biliary and hyperlipidemic groups in age, BMI, presence of precipitating factors, proportion of high-risk Down syndrome screening, fever, nausea/vomiting, abdominal pain, oliguria, oxygenation index, or activities of daily living scores ($P > 0.05$). However, the biliary group had a significantly longer time from onset to presentation, smaller gestational age at admission, more previous pregnancies, and lower proportions of diarrhea and cessation of defecation compared to the hyperlipidemic group ($P < 0.05$).

Disease Severity

In the biliary group, 12 cases (44.44%) were MAP and 15 cases (55.56%) were SAP. In the hyperlipidemic group, 9 cases (42.86%) were MAP and 12 cases (57.14%) were SAP. There was no statistically significant difference in disease severity between the two groups ($\chi^2 = 0.012$, $P = 0.912$).

Laboratory Findings

There were no statistically significant differences between the biliary and hyperlipidemic groups in white blood cell count, aspartate aminotransferase, albumin, blood urea nitrogen, blood glucose, potassium, D-dimer, or procalcitonin levels ($P > 0.05$). However, the biliary group had significantly lower levels of hemoglobin, platelets, C-reactive protein, cholesterol, and triglycerides, while showing higher levels of total bilirubin, direct bilirubin, alanine transaminase, alkaline phosphatase, glutamyl transpeptidase, creatinine, calcium, sodium, serum amylase, and N-terminal pro-brain natriuretic peptide compared to the hyperlipidemic group ($P < 0.05$).

Maternal Outcomes

The biliary group had a significantly shorter gestational age at delivery compared to the hyperlipidemic group ($P < 0.05$). There were no statistically signif-

ificant differences in premature delivery rate, cesarean section rate, or artificial intervention termination of pregnancy rate between the two groups ($P>0.05$). All maternal patients were cured and discharged, with no deaths.

Neonatal Outcomes

Among the 48 APIP patients, 42 delivered during hospitalization (21 in the biliary group and 21 in the hyperlipidemic group). Neonates in the biliary group had significantly lower birth weight and shorter birth length compared to the hyperlipidemic group. The incidences of pathological jaundice, respiratory distress, and ventilator-assisted breathing were also significantly higher in the biliary group ($P<0.05$). There were no statistically significant differences in head circumference, Apgar scores, hospitalization rate, pneumonia incidence, or fetal mortality between the two groups ($P>0.05$). There were 3 fetal deaths, yielding a mortality rate of 7.14% (3/42), all occurring in the biliary group, though the difference in mortality between groups was not statistically significant.

Discussion

Etiology and Pathogenesis of APIP

Current domestic and international reports indicate that the etiologies of APIP are not significantly different from those of AP in the general population, with the top three causes remaining biliary, hyperlipidemic, and alcohol-related [8-9]. However, the ranking of these etiologies varies across studies. Most European and American countries report that APIP is primarily biliary in origin [10-11], accounting for over 50% of cases [12-14], while some domestic scholars have shown that hyperlipidemia is the main cause of APIP [15]. Our study found that biliary etiology accounted for 56.25% (27/48) and hyperlipidemic etiology accounted for 43.75% (21/48), with biliary disease remaining the most common cause. This aligns with European and American reports, possibly because our study population is from a city with higher economic status where greater attention is paid to dietary adjustments during pregnancy, resulting in a lower proportion of hyperlipidemia-induced APIP compared to studies from other Chinese cities.

The specific mechanisms by which biliary disease and hyperlipidemia cause APIP during pregnancy are not yet fully understood. Biliary disease may contribute to APIP through several mechanisms: (1) as pregnancy progresses, the enlarging uterus compresses the duodenum and biliary tract, slowing bile emptying; (2) increased progesterone during pregnancy relaxes gallbladder smooth muscle and inhibits biliary system contraction, further slowing bile emptying; (3) pre-pregnancy weight gain and insulin resistance cause bile stasis and increase the probability of gallstones; and (4) Chinese pregnant women, particularly in the second and third trimesters, often consume high-fat diets that increase bile and pancreatic exocrine secretion, further contributing to bile stasis. These combined factors increase bile secretion, concentration, and delayed

emptying, thereby increasing the risk of APIP [16]. Blood lipid levels during pregnancy are significantly higher than in non-pregnant individuals, reaching 2-4 times early pregnancy levels in the third trimester, possibly related to dietary habits and changes in progesterone levels [17]. As blood lipid levels increase, so does the risk of AP [18], potentially due to acute fat embolism and microcirculatory obstruction in pancreatic small vessels caused by large amounts of free fatty acids, as well as mitochondrial swelling and necrosis in pancreatic exocrine cells leading to pancreatic injury [19-23].

Clinical Characteristics of APIP by Etiology

Previous studies have reported that hyperlipidemic APIP is more severe than biliary APIP, more likely to progress to moderate-to-severe disease, and has higher probabilities of complications such as pancreatic pseudocysts, walled-off necrosis, and respiratory and circulatory system failure [24-25]. Our study found no difference in the probability of progression to SAP between the hyperlipidemic and biliary groups, possibly due to our small sample size. We found that the biliary group had more previous pregnancies and smaller gestational age at presentation, suggesting that increased gravidity may elevate the risk of biliary pancreatitis and that biliary pancreatitis is more likely to occur in pregnant women at earlier gestational ages. The specific mechanisms remain unclear and require further investigation.

Due to different etiologies, the biliary and hyperlipidemic groups showed distinct differences in laboratory indicators. Biliary pancreatitis may involve biliary obstruction and affect liver function, resulting in characteristic laboratory findings such as more pronounced elevations in bilirubin, alanine transaminase, alkaline phosphatase, and glutamyl transpeptidase, which may not be prominent in the hyperlipidemic group. Conversely, the hyperlipidemic group showed more significant elevations in lipid metabolism indicators such as cholesterol and triglycerides. Our results are consistent with these patterns. In hyperlipidemic acute pancreatitis, serum amylase is often not significantly elevated, possibly due to inhibition of amylase activity by lipoproteins. Our study confirmed this difference, with serum amylase being lower in the hyperlipidemic group than in the biliary group, reminding clinicians not to rely solely on the magnitude of serum amylase elevation for diagnosis and severity assessment in hyperlipidemic cases, but rather to combine clinical manifestations and multi-organ function for comprehensive evaluation.

Impact on Maternal Pregnancy Outcomes

Due to the effects of AP on organ function, maternal placental blood perfusion decreases dramatically, and maternal blood becomes hypercoagulable due to insufficient volume. Additionally, inflammatory factors activate the coagulation system, leading to fibrinogen deposition and microvascular embolism formation in chorionic capillaries, which exacerbates placental circulatory disturbances and causes severe uterine and placental ischemia and hypoxia. This may result

in maternal miscarriage or preterm delivery [26]. Since biliary pancreatitis is more likely to involve biliary infection and even systemic infection, this effect is particularly pronounced in the biliary group. Our study also found that the biliary group had a significantly shorter gestational age at delivery compared to the hyperlipidemic group.

APIP itself is not an indication for pregnancy termination, but reducing abdominal pressure is beneficial for controlling AP. Determining the indications for pregnancy termination is often complex. It is generally recommended to terminate pregnancy promptly in cases of severe APIP, no significant improvement after 24-48 hours of treatment, fetal distress, full-term pregnancy, or imminent miscarriage/preterm labor symptoms [27-28]. In our study, 27 patients underwent artificial pregnancy termination, all via cesarean section (16 cases [59.26%] in the biliary group and 11 cases [52.38%] in the hyperlipidemic group), with no statistically significant difference in termination rates between groups. This requires verification with larger sample sizes. Due to timely diagnosis and intervention, there were no maternal deaths in our study, and all patients were cured and discharged.

Impact on Fetal Outcomes

APIP adversely affects fetal outcomes, though few previous studies have comprehensively evaluated neonatal status in APIP patients with different etiologies. Our study comprehensively assessed neonatal outcomes by examining birth weight, length, head circumference, Apgar scores, need for hospitalization, presence of pathological jaundice, neonatal pneumonia, respiratory distress, and need for ventilator-assisted breathing. We found that neonates in the biliary group had lower birth weight and shorter birth length, with higher incidences of pathological jaundice, respiratory distress, and need for ventilator-assisted breathing compared to the hyperlipidemic group.

Previous studies have reported fetal mortality rates of 60% in APIP, though this may have decreased recently due to improved diagnosis and treatment [9,29-30]. In our study, 42 patients delivered during hospitalization, with 3 fetal deaths (7.14% mortality rate, 3/42), all occurring in the biliary group, though the difference in mortality between groups was not statistically significant. These results suggest that biliary etiology causes more severe fetal outcomes in APIP patients compared to hyperlipidemic etiology, alerting clinicians to more promptly and comprehensively assess fetal status and timely determine indications for pregnancy termination when managing biliary APIP patients.

Conclusion

In summary, APIP is a critical emergency with high fetal mortality. Only through early detection, early diagnosis, early assessment, and strict, accurate determination of indications and timing for pregnancy termination can maternal and fetal outcomes be improved. Our study found that biliary factors remain the

most common cause of APIP currently. For maternal outcomes, biliary APIP can significantly shorten gestational age at delivery. For fetal outcomes, the biliary group caused more severe complications than the hyperlipidemic group, including low birth weight and more severe organ complications. This serves as a clinical warning that biliary APIP patients require earlier comprehensive assessment of maternal and fetal status to reduce complications and improve outcomes. However, this study is a single-center retrospective study with a small sample size, which has certain limitations. We hope that larger-scale, multi-center prospective studies will further validate these findings to improve the clinical diagnosis and treatment of APIP.

Author Contributions: XU Jun conceived the research idea, designed the study, proposed the research question and methodology, performed statistical analysis, and drafted the manuscript; QI Wenjie implemented the research process; WANG Chao selected study subjects and collected sample data; HU Nan prepared tables and figures; MIAO Bin revised the final version and took responsibility for the manuscript.

Conflict of Interest: The authors declare no conflict of interest.

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