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ORIGINAL ARTICLE

Retrospective Study

Assessment of early factors for identification or prediction severe acute pancreatitis in pregnancy

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Abstract

BACKGROUND

Acute pancreatitis in pregnancy (APIP) is a rare and serious condition, and severe APIP (SAPIP) can lead to pancreatic necrosis, abscess, multiple organ dysfunction, and other adverse maternal and infant outcomes. Therefore, early identification or prediction of SAPIP is important.

AIM

To assess factors for early identification or prediction of SAPIP.

METHODS

The clinical data of patients with APIP were retrospectively analyzed. Patients were classified with mild acute pancreatitis or severe acute pancreatitis, and the clinical characteristics and laboratory biochemical indexes were compared between the two groups. Logical regression and receiver operating characteristic curve analyses were performed to assess the efficacy of the factors for identification or prediction of SAPIP.

RESULTS

A total of 45 APIP patients were enrolled. Compared with the mild acute pancreatitis group, the severe acute pancreatitis group had significantly increased ($P < 0.01$) heart rate (HR), hemoglobin, neutrophil ratio (NEUT%), and neutrophil–lymphocyte ratio (NLR), while lymphocytes were significantly decreased ($P < 0.01$). Logical regression analysis showed that HR, NEUT%, NLR, and lym-

phocyte count differed significantly ($P < 0.01$) between the groups. These may be factors for early identification or prediction of SAPIP. The area under the curve of HR, NEUT%, NLR, and lymphocyte count in the receiver operating characteristic curve analysis was 0.748, 0.732, 0.821, and 0.774, respectively. The combined analysis showed that the area under the curve, sensitivity, and specificity were 0.869, 90.5%, and 70.8%, respectively.

CONCLUSION
HR, NEUT%, NLR, and lymphocyte count can be used for early identification or prediction of SAPIP, and the combination of the four factors is expected to improve identification or prediction of SAPIP.

Key Words: Severe acute pancreatitis in pregnancy; Early identification factors; Early predictive factors; Clinical features; Laboratory biochemical index

Core Tip: This retrospective study explored factors for early identification or prediction of severe acute pancreatitis in pregnancy (SAPIP). A total of 45 APIP patients were enrolled. Logistic regression analysis showed that heart rate, neutrophil ratio, neutrophil–lymphocyte ratio, and lymphocyte count were significantly correlated with SAPIP. These four indexes showed valuable area under the curve, sensitivity, and specificity through receiver operating characteristic curve analysis. These results suggested that heart rate, neutrophil ratio, neutrophil-lymphocyte ratio, and lymphocyte count can be used for early identification or prediction of SAPIP.

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INTRODUCTION

Acute pancreatitis in pregnancy (APIP) is a rare but serious condition, and the incidence is reported to be between 1/12000 and 1/1000[1-3]. Although APIP is rare in the clinic, it may be associated with high maternal mortality and fetal loss[4-6], and it has been shown increasing attention by researchers.

Previous studies have shown that severe APIP (SAPIP) is significantly associated with a high risk of maternal and fetal death[7,8]; therefore, early identification and prediction of SAPIP, as well as timely and appropriate management, are critical to fetal and maternal prognosis. There are currently several scoring systems used to assess AP severity[9]. Many hematological changes occur in women during pregnancy, so APIP has some special clinical features in addition to the characteristics of general pancreatitis. Therefore, these scores may not accurately assess and predict the severity of APIP [10,11]. Better indicators for early identification and prediction of APIP severity are needed. Some studies suggested that the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio, erythrocyte distribution width-platelet ratio, γ-glutamyl transpeptidase, lipase, high-density lipoprotein, platelet volume, lactate dehydrogenase, triglyceride, and cholesterol may be predictors of APIP[12-15]. However, there are few reports on the early identification and prediction of SAPIP.

Based on 45 clinical cases of APIP from the Department of Critical Care Medicine, Maternal and Child Health Hospital of Hubei Province and Department of Biliary-Pancreatic Surgery, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, this retrospective study identified multiple factors associated with SAPIP. Clinical parameters were compared between patients with mild APIP (MAPIP) and those with SAPIP. These are expected to facilitate the timely identification and prediction of SAPIP.

MATERIALS AND METHODS

Study subjects and definitions

A retrospective study was conducted on APIP patients admitted to the Department of Critical Care Medicine, Maternal and Child Health Hospital of Hubei Province and Department of Biliary–Pancreatic Surgery, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology from 2017 to 2020. Due to the difficulty in obtaining data for patients before admission, data were only collected for the first examination within 24 h after hospitalization. Information on maternal age, gestational age at onset, potential causes of AP, clinical manifestations and complications, laboratory data, and maternal and fetal outcomes were collected from patient medical records.

We defined APIP as AP that occurred during pregnancy and the 42-d postpartum period. Diagnosis of AP needs to meet at least two of the following three characteristics on the basis of the Revised Atlanta criteria[16]: (1) Acute persistent epigastric pain; (2) Serum amylase and/or lipase increased by > 3 times the upper limit of normal; and (3) Abdominal imaging findings consistent with AP. Based on the Revised Atlanta criteria[16], AP was classified into three categories according to severity: (1) Mild AP (MAP), pancreatitis without organ dysfunction or systemic complications; (2) Moderately severe AP (MSAP), pancreatitis with persistent organ dysfunction or local/systemic complications within 48 h of starting treatment; and (3) Severe AP (SAP), persistent pancreatitis dysfunction or local/systemic complications.

Patients with chronic pancreatitis and patients with missing data were excluded from the study. We enrolled 45 patients with APIP. Due to the small number of cases of MSAP in this study, patients were divided into two groups: MAP and SAP (including MSAP and SAP). There were 24 cases of MAP and 21 cases of SAP. The study was approved by the Ethics Committee of Hubei Maternal and Child Health Care Hospital and Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology. Technical records. Data did not include potential patient identifying information and therefore did not require informed consent.

Statistical analysis

SPSS 17.0 was used for data analysis. The measurement data of normal distribution were expressed as mean ± standard deviation, and *t* test of two independent samples was used for comparison between groups. Measurement data with non-normal distribution were expressed as median (interquartile range), and the nonparametric Mann–Whitney *U* test was used for comparison between groups. The numerical data were expressed as frequency, and groups were compared by Fisher's exact test. Logistic regression analysis was performed on the variables with significant differences between the groups to analyze the factors associated with SAPIP. Receiver operating characteristic curve (ROC) was plotted to evaluate the predictive efficiency of each indicator.

RESULTS

General clinical features

The 45 patients had a mean age of 30.0 ± 3.8 years (range: 22-37 years). According to the etiology, there were 18 cases (40.0%) of hypertriglyceridemia, 11 cases (24.44%) of cholelithiasis (24.44%), and 16 cases (35.56%) of other diseases. APIP patients included 4 cases (10.26%) in the first trimester, 9 cases (20.51%) in the second trimester, and 32 cases (69.23%) in the third trimester. There were no maternal deaths, but fetal loss occurred in 6 cases. In the initial hospitalization, 13 cases were diagnosed as severe; 4 cases had acute respiratory distress syndrome, and 5 cases had shock symptoms. Acidosis and renal dysfunction occurred in 2 cases and liver failure in 2 cases. Eight cases became severe after hospitalization; 3 cases had renal dysfunction, 3 cases had pancreatic hemorrhage and necrosis, and 2 cases had acute respiratory distress syndrome and liver failure. Due to the small sample size, there may have been errors in individual analysis, so the two groups were studied as a whole in the following study.

Differences in general clinical features between MAPIP and SAPIP

We mainly compared the general clinical characteristics of MAPIP with SAPIP, including underlying etiology, pregnancy stage, age, heart rate (HR), and blood pressure. There were no significant differences in underlying etiology and pregnancy stage between the two groups (Tables 1 and 2). There were also no significant differences in age and blood pressure (Table 3). HR in the severe group was significantly higher than in the mild group ($P < 0.01$) (Table 3).

Differences in laboratory biochemical indicators between MAPIP and SAPIP

Whole blood was collected to compare the laboratory biochemical indicators. Hemoglobin and neutrophil ratio (NEUT%) in the SAPIP group were significantly higher than in the MAPIP group ($P < 0.01$) (Table 4). The total number of lymphocytes in the SAPIP group was significantly lower than that in the MAPIP group ($P < 0.01$). NLR in the SAPIP group was significantly higher than in the MAPIP group ($P < 0.01$) (Table 4).

Assessment of factors associated with SAPIP

Logistic regression analysis was performed on HR, hemoglobin, NEUT%, lymphocyte count, and NLR, which were significantly different between the MAPIP and SAPIP groups. HR, NEUT%, lymphocyte count, and NLR were significantly correlated with severity of APIP ($P < 0.01$), but hemoglobin was not ($P > 0.01$) (Table 5). ROC curves showed the early recognition or predictive efficiency of each relevant factor (Table 6 and Figure 1A). NLR had the largest area under the curve (AUC) (0.821). To evaluate whether their combination was more effective, ROC curve analysis was performed on the four factors. AUC for combined detection was 0.869, sensitivity was up to 90.5%, and specificity was up to 70.8% (Figure 1B).

DISCUSSION

We reported the value of combining detection of vital signs and laboratory biochemical indicators in early identification or prediction of SAPIP after hospitalization. Compared with the MAPIP group, HR, NEUT%, and NLR were significantly higher in the SAPIP group, while lymphocyte count was significantly reduced in the SAPIP group. To assess whether

Table 1 Differences in etiology

Etiology	MAPIP, *n* = 24	SAPIP, *n* = 21	Test value	*P* value
Hypertriglyceridemia	6	12	χ^2 = 4.890	0.087[1]
Biliary	7	4		
Other causes	11	5		

[1]Pearson's χ^2 test. MAPIP: Mild acute pancreatitis in pregnancy; SAPIP: Severe acute pancreatitis in pregnancy.

Table 2 Differences during pregnancy stage

Pregnancy stage	MAPIP, *n* = 24	SAPIP, *n* = 21	*P* value
First trimester	2	2	0.258[1]
Second trimester	7	2	
Late trimester	15	17	

[1]Fisher's exact test. MAPIP: Mild acute pancreatitis in pregnancy; SAPIP: Severe acute pancreatitis in pregnancy.

Table 3 Differences in age, heart rate, and blood pressure

Factors	MAPIP, *n* = 24	SAPIP, *n* = 21	Test value	*P* value
Age in yr	28.82 ± 4.50	30.40 ± 4.10	*t* = 0.521	0.605[1]
Heart rate in bpm	88.0 (19.75)	120.0 (40.0)	z = -2.849	0.004[2]
Systolic blood pressure in mmHg	115.67 ± 11.89	119.57 ± 11.82	*t* = -1.102	0.277[1]
Diastolic blood pressure in mmHg	73.21 ± 9.48	76.24 ± 9.16	*t* = -1.087	0.283[1]

Data are *n* (%).
[1]*T*-test of two independent samples.
[2]Mann–Whitney nonparametric test.
MAPIP: Mild acute pancreatitis in pregnancy; SAPIP: Severe acute pancreatitis in pregnancy.

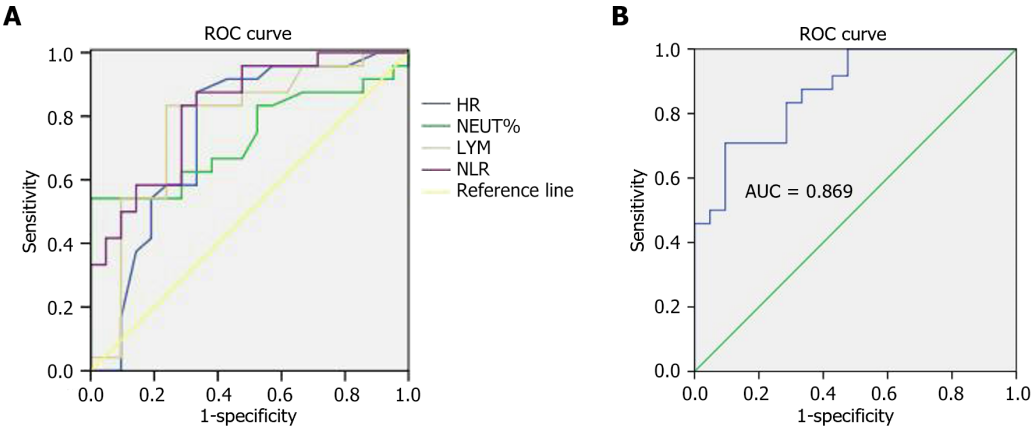

Figure 1 Specificity and sensitivity of heart rate, neutrophil ratio, lymphocyte count, and neutrophil-lymphocyte ratio were analyzed by receiver operating characteristic curve. A: Analysis of individual factors; B: Analysis of combination of factors. HR: Heart rate; LYM: Lymphocyte count; NEUT%: Neutrophil ratio; NLR: Neutrophil–lymphocyte ratio; ROC: Receiver operating characteristic.

Table 4 Comparison of the first laboratory biochemical indicators after admission

Factor	MAPIP, *n* = 24	SAPIP, *n* = 21	Test value	*P* value
RBC as × 10^{12}	3.53 ± 0.48	3.95 ± 0.75	*t* = -2.275	0.028
HCT	33.40 ± 5.65	36.99 ± 5.14	*t* = -2.219	0.032
HGB in g/L	110.67 ± 17.49	127.71 ± 22.68	*t* = -3.003	0.004
RDW	13.45 (1.12)	13.80 (2.35)	*z* = -1.298	0.194
WBC as × 10^{9}	12.42 ± 5.02	15.08 ± 5.55	*t* = -1.688	0.099
NEUT as × 10^{9}	11.18 ± 4.81	14.66 ± 4.81	*t* = -2.422	0.02
NEUT%	83.84 ± 8.44	90.14 ± 3.52	*t* = -3.183	0.003
LYM as × 10^{9}	1.23 (0.46)	0.58 (0.51)	*z* = -3.141	0.002
NLR	8.12 (9.80)	27.43 (25.61)	*z* = -3.686	0
TG in mmol/L	2.63 (6.80)	19.05 (31.49)	*z* = -2.207	0.027
TC in mmol/L	5.26 (2.41)	14.32 (14.29)	*z* = -1.615	0.106
Ca in mmol/L	2.13 (0.15)	2.04 (0.38)	*z* = -0.854	0.393
AMY in U/L	387 (1450.00)	588 (763.60)	*z* = -0.375	0.707
BUN in mmol/L	3.06 (1.12)	2.16 (2.75)	*z* = -0.797	0.426
SCR in mg/dL	47.66 (13.17)	47.45 (17.55)	*z* = 0.046	0.946
GPT in U/L	8.90 (16.00)	8.30 (33.10)	*z* = -0.194	0.846
GOT (U/L)	17.85 (21.73)	18.00 (28.50)	*z* = -0.546	0.585
DBIL in μmol/L	3.25 (2.43)	3.40 (4.45)	*z* = -0.046	0.964
IBIL in μmol/L	7.42 (3.80)	7.46 (4.37)	*z* = -0.032	0.975

AMY: Amylase; BUN: Blood urea nitrogen; DBIL: Direct bilirubin; GOT: Glutamic oxaloacetic transaminase; GPT: Glutamic pyruvic transaminase; HCT: Hematocrit value; HGB: Hemoglobin; IBIL: Indirect bilirubin; LYM: Lymph; MAPIP: Mild acute pancreatitis in pregnancy; NEUT: Neutrophil; NEUT%: Neutrophil ratio; NLR: Neutrophil–lymphocyte ratio; RBC: Red blood cell; RDW: Red blood cell distribution width; SAPIP: Severe acute pancreatitis in pregnancy; SCR: Serum creatinine; TC: Total cholesterol; TG: Triglyceride; WBC: White blood cell.

Table 5 Logistic regression analysis of related factors

Factor	OR	95%CI	*P* value
Heart rate in bpm	1.052	1.016–1.090	0.004
Hemoglobin in g/L	1.046	1.009–1.048	0.014
NEUT%	1.179	1.043–1.333	0.009
LYM as × 10^{9}	0.095	0.019–0.483	0.005
NLR	1.121	1.045–1.202	0.001

CI: Confidence interval; LYM: Lymphocyte count; NEUT%: Neutrophil ratio; NLR: Neutrophil-lymphocyte ratio; OR: Odds ratio.

these indicators can be used as factors for identification or prediction of SAPIP, ROC analysis was performed for HR, NEUT%, lymphocyte count, and NLR. The AUC for combined analysis of the four indicators was 0.869, sensitivity was 90.5%, and specificity was 70.8%. Therefore, combined detection of the four indicators is helpful for early identification or prediction of SAPIP.

SAPIP seriously threatens the health and life of pregnant women and fetuses[17-19]. Due to the lack of indicators for early identification or prediction of SAPIP, most previous studies have determined some laboratory detection indicators for predicting APIP by comparing APIP patients with normal pregnant women[13,14]. Some studies compared SAP with MAP and MSAP to explore the indicators related to APIP severity, but only laboratory data were selected for the indicators[20,21]. Our study also included vital signs such as HR and blood pressure, which could have made the assessment more comprehensive.

Table 6 Assessment of the effectiveness of relevant factors

Factors	AUC	95%CI	*P* value	Cutoff	Sensitivity, %	Specificity, %
HR in bpm	0.748	0.593-0.903	0.004	107.000	66.7	87.5
NEUT%	0.732	0.582-0.882	0.008	84.300	100	54.2
LYM as $\times 10^9$	0.774	0.628-0.920	0.002	0.875	83.3	76.2
NLR	0.821	0.700-0.943	0.000	17.890	71.4	83.3

AUC: Area under the curve; CI: Confidence interval; HR: Heart rate; NEUT%: Neutrophil ratio; LYM: Lymphocyte count; NLR: Neutrophil–lymphocyte ratio.

Many studies have shown that lymphocytes are involved in the inflammatory response of AP[22-25]. Studies showed that the lymphocyte DNA damage in AP patients was significantly higher than that in the control groups, especially the high level of lymphocyte DNA damage in SAP patients[26]. Patients with persistently low lymphocyte counts in the early stage of AP are more likely to develop infectious pancreatic necrosis (IPN), which can predict the severity of AP and the development of IPN, and it is important for early diagnosis and timely intervention[27]. The role of the lymphocyte count in predicting APIP has not been reported previously. In our study, we reported a significantly reduced lymphocyte count with a higher AUC (0.774), second only to NLR. If the threshold value was 0.875 × 10^9, the sensitivity was 83.3%, suggesting that lymphocyte count could be one of the best predictors of SAPIP.

Although the detailed mechanism of the relationship between neutrophils and AP has not been elucidated, some studies suggest that neutrophils play an important role in the exacerbation of AP, possibly through the neutrophilic extracellular trap pathway[28-30]. Studies have shown that elevated neutrophils are associated with complications such as pancreatic infection and necrosis and pseudocyst formation and can be used as a predictor of AP complications[31]. The critical value for predicting the occurrence of IPN is > 9.47 × 10^9, with sensitivity up to 69.09% and specificity up to 60.74%[32]. In our study, we reported that blood neutrophil count was correlated with APIP severity, and the best diagnostic threshold for predicting severe pancreatitis was 84.30%, with sensitivity up to 100% and specificity up to 54.20%, which could be used as one of predictors of SAPIP.

NLR is a more comprehensive biomarker that uses neutrophil and lymphocyte counts to respond quickly to the extent of inflammation progression and serves as a useful predictor for identifying the severity of AP[33-36]. Meta-analysis showed that the AUC of NLR for predicting the severity of pancreatitis was 0.82, indicating that it had a moderately high predictive value[34]. In APIP, İlhan *et al*[12] reported in 2015 that NLR may have a role in prediction of disease severity with a sensitivity of 78.6% and specificity of 62.1%. However, the predictive value of NLR reported in the literature is inconsistent[37]. Some authors have suggested that NLR alone may not be a true indicator of the severity of AP because it is affected by treatment drugs and waiting period prior to analysis[37]. In our study, NLR could be used as a valuable factor for identification or prediction of SAPIP with sensitivity of 71.40% and specificity of 83.30%.

SAP can cause tachycardia through metabolic disorders, vagal reflex, hemodynamic instability, myocarditis, and other mechanisms[38]. Tachycardia includes sinus tachycardia, supraventricular tachycardia, and ventricular tachycardia; among which, sinus tachycardia is the most common[39]. The role of HR in early recognition/prediction of SAP has not been reported. In our study, HR in the SAPIP group was significantly higher than in the MAPIP group. The best diagnostic threshold for predicting severe pancreatitis was 107 bpm, sensitivity was 66.7%, and specificity was 87.5%. It could be used for identification or prediction of SAPIP.

Our study had several limitations. First, we included only patients with complete APIP records at the two centers, and some patients who were not admitted were excluded from the analysis. Therefore, a larger, multicenter prospective study is needed to validate these results. Second, due to the small number of MSAP cases, their inclusion in the SAP group may have biased the data of the SAP group. Third, due to the small size of the overall sample, the time of onset of severe disease was not classified, so early identification and prediction were not analyzed separately.

CONCLUSION

We identified HR, NEUT%, and NLR as independent factors for early identification or prediction of SAPIP. Combined detection with the four factors can help improve early prediction and identification, which can help to determine treatment management and improve outcomes.

FOOTNOTES

Author contributions: Tian R and Shi CJ conceptualized and designed the research; Mei LF, Gan Q, Hu J, and Li YX screened patients and acquired clinical data; Mei LF, Tian R, and Shi CJ performed the data analysis; Mei LF, Tian R, and Shi CJ wrote the paper; All authors read and approved the final manuscript. Mei LF acquired clinical data, performed data analysis, and prepared the first draft of the manuscript. She has made crucial and indispensable contributions towards the completion of the project and thus qualified as one of the

first authors of the paper. Both Tian R and Shi CJ have played important and indispensable roles in the research design, data interpretation, and manuscript preparation as the co-corresponding authors. Shi CJ conceptualized, designed, and supervised the whole process of the project. He searched the literature and revised and submitted the early version of the manuscript. Tian R was instrumental and responsible for data re-analysis and re-interpretation, figure plotting, the comprehensive literature search, and preparation and submission of the current version of the manuscript. This collaboration between Tian R and Shi CJ was crucial for the publication of this manuscript.

Institutional review board statement: The study was reviewed and approved by the Ethics Committee of Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology and the Ethics Committee of Maternal and Child Health Hospital of Hubei Province (Approval No.: TJ-IRB202404002 and 2023IEC097).

Informed consent statement: Technical records and data did not include potential patient identifying information and therefore did not require informed consent.

Conflict-of-interest statement: All authors have no conflicts of interest to declare.

Data sharing statement: No additional data are available.

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