

Neutrophil to Lymphocyte Ratio as an Early Prognostic Predictive Marker in Patients with Acute Pancreatitis: An Observational Study**Gauravh Raath¹, Om Kumar Sharma², Ashish Singh³, Abhishek Singh Rathore⁴**¹Junior Resident, Department of Surgery, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh India²Associate Professor, M.S General Surgery, Department of Surgery, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh India³Assistant Professor, M.S General Surgery, Department of Surgery, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh India⁴Associate Professor, M.S General Surgery, Department of Surgery, Rohilkhand Medical College and Hospital Bareilly, Uttar Pradesh India

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Conflict of interest: Nil

Abstract:

Introduction: The pancreas is an important part of the gastrointestinal system because it digests food and produces enzymes that break down fats. Acute pancreatitis is an inflammatory illness characterised by the death of acinar cells and inflammation in both the local and systemic domains. The disease ranges from mild to severe. The Neutrophil-Lymphocyte ratio (NLR) is an effective predictive indicator in acute pancreatitis, showing cellular immunological activation, stress, and systemic inflammation. This study intends to fill a gap in research on NLR in acute pancreatitis in India, allowing for better disease management and timely intervention.

Aim: To determine the Neutrophil to lymphocyte ratio (NLR) among acute pancreatitis patients and evaluate its prognostic significance.

Methods: The study was conducted on 227 patients, where patient data was collected on day 0, 1 and 2 and analysed for the viability of the neutrophil to lymphocyte ratio in predicting the adverse effects of AP.

Results: The study had the following findings.

1. The proportion of males having AP (84.58%) was higher than females (15.42%).
2. Mean age for AP was 42 years.
3. The severity among patients was mild (150) and severe (40).
4. Change from Day 0 to day 2 was only significant in severe category of Atlanta classification.

Conclusions: My study has shown that NLR is a reliable indicator of necrosis in situations of acute pancreatitis. As a basic investigation, it incurs no additional fees for the patient. NLR has a high association with the prediction of necrosis in patients of acute pancreatitis. Consistent daily observation will provide a dynamic represent of the host's immune response to pancreatitis, allowing for the prediction of necrosis in the patient. The NLR ratio evaluates the severity of acute pancreatitis on multiple days (day 0, 1, 2) and predicts the patient's prognosis and outcome in terms of acute pancreatitis.

Keywords: Acute Pancreatitis, Neutrophil to Lymphocyte Ratio, NLR, Prognostic Marker, Predictive Marker, Amylase Levels, Lipase Levels.

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Introduction

Acute pancreatitis is a condition involving inflammation of the pancreas, impacting both local and systemic functions. The pancreas, crucial in digestion, has dual roles: exocrine (producing enzymes) and endocrine (regulating blood sugar). [1] Acute pancreatitis can be triggered by factors like gallstones, alcohol, certain medications, and with rising global incidence linked to obesity. [2] Acute pancreatitis has a variety of presentation and the severity of the disease can range from a mild

attack in which the recovery is good to severe where the result can be fatal. Mortality has decreased due to better diagnosis and treatment, yet morbidity continues to be significant. Initial acinar cell damage leads to local inflammation and systemic inflammatory response syndrome (SIRS), possibly progressing to multi-organ dysfunction syndrome (MODS).[2] Diagnosis involves criteria like elevated pancreatic enzymes (amylase, lipase), abdominal discomfort, and imaging abnormalities.

[3] Various grading systems aid in severity assessment (e.g., Ranson's criteria, APACHE, BISAP).⁴ New prognostic tools like Neutrophil-Lymphocyte Ratio (NLR) are being explored due to their predictive accuracy in acute pancreatitis, reflecting systemic inflammation and aiding in early detection of complications. [7] NLR, calculated from neutrophil and lymphocyte counts, serves as a marker for immune response and inflammation in many medical conditions. Elevated NLR correlates with severe acute pancreatitis, providing additional prognostic insight beyond traditional scoring systems. Its clinical utility lies in its ability to predict outcomes and guide timely interventions. [7]

In conclusion, understanding NLR's role in acute pancreatitis may refine clinical pathways, enhancing management strategies and prognostic assessment, although limitations exist for late-presenting patients. [8] Further research, including in regions like India, aims to address these gaps and optimize care for this complex condition.

Aim:

To determine the Neutrophil to lymphocyte ratio (NLR) among acute pancreatitis patients and evaluate its prognostic significance.

Material and Method

Place of Study: Rohilkhand Medical College and Hospital, Bareilly, U.P.

Type of Study: Observational study.

Study Duration: 1st November 2022 – 31st October 2023.

Subjects: All patients who are diagnosed with acute pancreatitis.

Inclusion Criteria: All cases of acute pancreatitis admitted in our hospital during the study period.

Exclusion Criteria:

1. Patients with chronic pancreatitis
2. Patients with recurrent pancreatitis
3. Patients with pancreatic malignancy

Sample Size: A sample size of 227 was calculated using the formula $4pq/L^2$.

Method

The data obtained from the completed questionnaires were manually entered in Microsoft Excel (version - Office 365). The data was appropriately recoded for the Variables. The final sheet was imported into R version 4.2.3 using the "readxl" package and further analysis was done using packages like "tidyverse", "gtsummary", "flextable", "ggplot2", "ggstatsplot" and their dependencies. Continuous variables such as age, NLR were expressed in terms of median, interquartile range, maximum and minimum.

The outcome variables which were nominal expressed in terms of frequencies and percentages. Further Chi-square test or Fisher's test was used to find an association between categorical variables and the Wilcoxon rank-sum test and Welch two sample t. test was used for the continuous variables as per the normality of data

Observations

Table 1: Distribution of age with respect to sex of pancreatitis patients; N = 227

Types	Female, N = 35 (15.42%) ¹	Male, N = 192 (84.58%) ¹	Total, N = 227 ¹
Age (in years)			
Mean ± (SD)	41 ± (10)	42 ± (11)	42 ± (11)
Median (IQR)	41 (35, 47)	42 (33, 48)	41 (34, 48)
Range	24, 72	18, 70	18, 72
Age Groups			
< 20	0 (0%)	3 (1.6%)	3 (1.3%)
21 - 30	7 (20%)	31 (16%)	38 (17%)
31 - 40	10 (29%)	60 (31%)	70 (31%)
41 - 50	12 (34%)	59 (31%)	71 (31%)
51 - 60	4 (11%)	33 (17%)	37 (16%)
61 - 70	1 (2.9%)	6 (3.1%)	7 (3.1%)
> 70	1 (2.9%)	0 (0%)	1 (0.4%)
¹ n (%)			

Table 1 show that male proportion was 84.58% while female proportion was 15.42%. Overall Mean Age of patients was 42 having similar age in both groups.

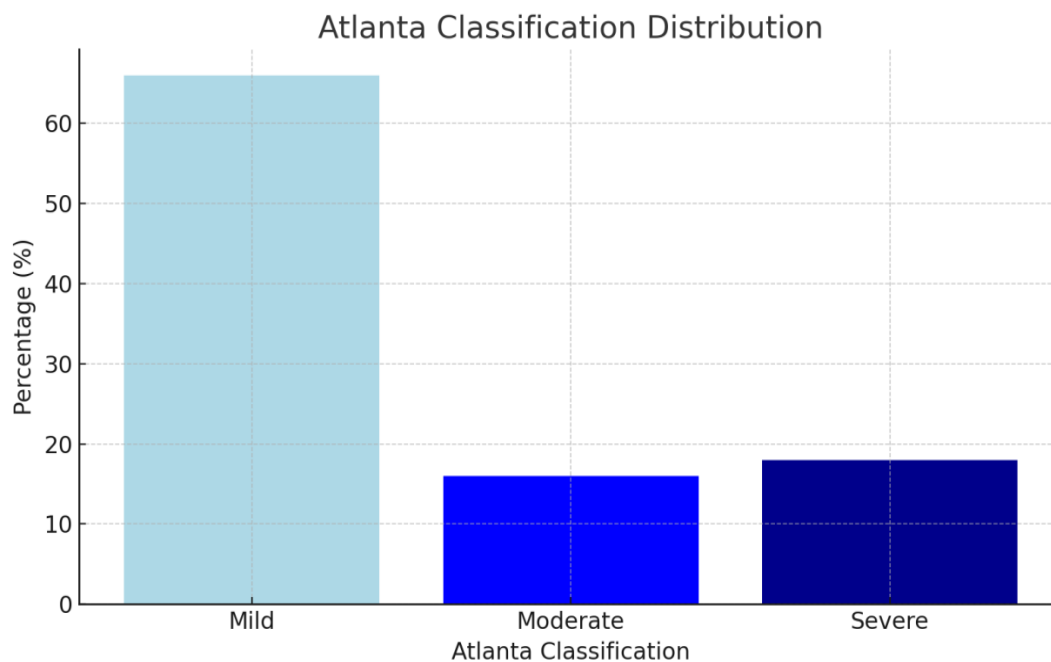


Figure 1: Distribution of severity of pancreatitis in patients as per Atlanta classification; N =227

Fig 1 shows the severity of pancreatitis in patients based on Atlanta Classification. Most Commonly Mild forms were present (66%).

Table 3: Characteristics of patients regarding days of hospital stays and outcome of disease during admission in form of death or discharge; N =227

Characteristic	N = 227 ¹
Days of Hospital Stay	
Mean ± (SD)	12 ± (7)
Median (IQR)	11 (6, 18)
Range	1, 27
Outcome	
Death	25 (11%)
Discharge	202 (89%)
¹ n (%)	

Table 3 shows that overall median days of hospital stay was 11 days with IQR of (6, 18) days. Overall, 11% of the patients died due to pancreatitis. Median stay in patients who died was lower (4) in comparison to patients who got discharged (12) and it was statistically significant.

Table 4: Distribution of NLR over 0 to 2nd day within patients; N = 227

Variable	Day 0, N = 227 ¹	Day 1, N = 227 ¹	Day 2, N = 227 ¹	p-value ²
NLR				0.3
Mean ± (SD)	4.8 ± (3.1)	6.3 ± (9.4)	5.8 ± (5.6)	
Median (IQR)	4.2 (3.0, 5.6)	4.1 (3.0, 6.5)	3.7 (2.6, 6.3)	
Range	0.4, 18.8	0.5, 96.0	0.6, 48.0	
NLR (categorized)				0.067
< 3	25 (11%)	16 (7.0%)	30 (13%)	
3 to 6	85 (37%)	77 (34%)	91 (40%)	
> 6	117 (52%)	134 (59%)	106 (47%)	
¹ n (%), ² Kruskal-Wallis rank sum test; Pearson's Chi-squared test				

Table 4 showing distribution NLR and its categories over 3 days. Median value at day 0 was 4.2 with IQR of 3.0 – 5.6, while 3.7 with IQR of 2.6 – 6.3 at day 2. There was increase in category (> 6) from day 0 (52%) to day 1 (59%) while decrease to day 2 (47%). It was not statistically significant with period of time.

Table 5: Distribution of NLR from day 0 to day 2 w.r.t Atlanta classification; N = 227

Variable	Mild, N = 150 ¹	Moderate, N = 37 ¹	Severe, N = 40 ¹	p-value ²
NLR at Day 0				<0.001
Mean ± (SD)	3.75 ± (2.00)	5.67 ± (2.31)	7.94 ± (4.42)	
Median (IQR)	3.13 (2.54, 4.50)	5.60 (4.21, 6.62)	6.62 (4.82, 10.34)	
Range	0.39, 15.50	1.75, 11.38	2.00, 18.80	
NLR at Day 1				<0.001
Mean ± (SD)	4.9 ± (10.8)	7.4 ± (3.7)	10.7 ± (4.8)	
Median (IQR)	3.6 (2.3, 4.4)	6.5 (5.1, 7.8)	9.2 (7.6, 13.4)	
Range	0.5, 96.0	2.7, 18.4	4.1, 23.3	
NLR at Day 2				<0.001
Mean ± (SD)	3.5 ± (2.4)	6.5 ± (4.4)	13.4 ± (7.9)	
Median (IQR)	3.1 (2.3, 4.2)	5.5 (4.2, 6.5)	11.3 (7.9, 16.2)	
Range	0.6, 18.6	2.0, 23.5	3.3, 48.0	
NLR categories at day 0				<0.001
< 3	23 (15%)	2 (5.4%)	0 (0%)	
3 to 6	72 (48%)	7 (19%)	6 (15%)	
> 6	55 (37%)	28 (76%)	34 (85%)	
NLR categories at day 1				<0.001
< 3	16 (11%)	0 (0%)	0 (0%)	
3 to 6	75 (50%)	2 (5.4%)	0 (0%)	
> 6	59 (39%)	35 (95%)	40 (100%)	
NLR categories at day 2				<0.001
< 3	29 (19%)	1 (2.7%)	0 (0%)	
3 to 6	82 (55%)	8 (22%)	1 (2.5%)	
> 6	39 (26%)	28 (76%)	39 (98%)	

¹n (%), ²Kruskal-Wallis rank sum test; Fisher's exact test

Table 5 showing distribution of NLR and its categories with respect to day and Atlanta classification. In Mild Atlanta classification median (IQR) NLR value was 3.13 (2.54, 4.50) on day 0, 3.6 (2.3, 4.4) on day 1 and 3.1 (2.3, 4.2) on day 2. While in severe category it was 6.62 (4.82, 10.34) on day 0 and 11.3 (7.9, 16.2) on day 2. In mild category all

three categories of NLR value patients were present, while in severe category of Atlanta classification, < 3 category was not present. NLR and its categories on each day were having statistically significant association with Atlanta Classification. Change from Day 0 to day 2 was only significant in severe category of Atlanta classification.

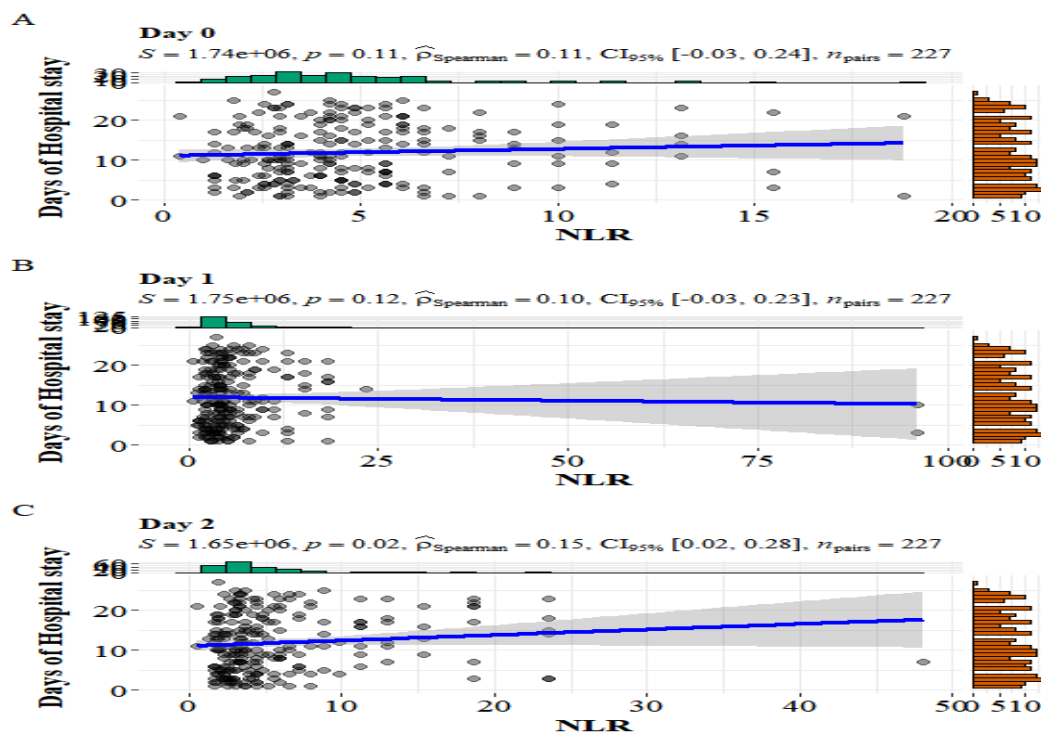


Figure 3: Scatter plot showing relation between NLR and number of days stayed at hospital; N = 227 Figure 1 shows that NLR at day 2 had statistically significant association with number of days stayed at hospital with p value of 0.02 with low effect size of 0.15. NLR at other days was not significantly associated.

Table 6: Distribution of NLR from day 0 to day 2 w.r.t Outcome; N = 227

Variable	Death, N = 25 ¹	Discharge, N = 202 ¹	p-value ²
NLR at Day 0			0.004
Mean ± (SD)	6.62 ± (4.22)	4.57 ± (2.84)	
Median (IQR)	4.82 (3.95, 7.25)	3.95 (2.81, 5.60)	
Range	1.30, 18.80	0.39, 18.80	
NLR at Day 1			0.010
Mean ± (SD)	7.5 ± (4.5)	6.2 ± (9.8)	
Median (IQR)	7.1 (4.1, 9.8)	4.1 (2.9, 6.3)	
Range	1.4, 18.4	0.5, 96.0	
NLR at Day 2			0.015
Mean ± (SD)	8.0 ± (6.7)	5.5 ± (5.4)	
Median (IQR)	6.0 (3.7, 8.8)	3.7 (2.6, 6.0)	
Range	1.6, 23.5	0.6, 48.0	
NLR categories at day 0			0.11
< 3	1 (4.0%)	24 (12%)	
3 to 6	6 (24%)	79 (39%)	
> 6	18 (72%)	99 (49%)	
NLR categories at day 1			0.2
< 3	1 (4.0%)	15 (7.4%)	
3 to 6	5 (20%)	72 (36%)	
> 6	19 (76%)	115 (57%)	
NLR categories at day 2			0.2
< 3	2 (8.0%)	28 (14%)	
3 to 6	7 (28%)	84 (42%)	
> 6	16 (64%)	90 (45%)	

¹n (%),²Wilcoxon rank sum test; Fisher's exact test

Table 6 showing distribution of NLR and its categories with respect to day and Outcome of disease. In patients who died, median (IQR) NLR value was 4.82 (3.95, 7.25) on day 0, 7.1 (4.1, 9.8) on day 1

and 6.0 (3.7, 8.8) on day 2. While in patients who got discharged it was 3.95 (2.81, 5.60) on day 0 and 3.7 (2.6, 6.0) on day 2. NLR values at each day were significantly associated with Outcome of dis-

ease. While none of the categories at any day were significantly associated with Outcome of disease. The change from Day 0 to day 2 was significant in patients who got discharged.

Discussion

Of the 227 individuals evaluated with acute pancreatitis, 84.58% were male and 15.42% were female. The observed occurrence can be related to the fact that males in our demographic consume more alcohol than females. Alcohol use has long been recognised as a significant risk factor for pancreatitis.

The age range of people with acute pancreatitis, which ranges from 18 to 72 years old, demonstrates the varied age presentation of this disease. The largest proportion of patients in this study are between the ages of 41 and 50, accounting for 31.3% of the total study population followed by 30.8% in 31 to 40 years range. These findings highlight the importance of knowing the epidemiology and risk factors associated with acute pancreatitis as people age. The high prevalence of pancreatitis is seen among people aged 31 to 50 years age which can be linked to the complicated interaction of several factors that contribute to the condition's occurrence in this population. It has been seen that lifestyle factors such as alcohol intake, smoking, and eating habits peak during the periods of young adulthood and middle age.

This is consistent with the age distribution revealed in the study. Furthermore, metabolic problems such as obesity and metabolic syndrome, which are known risk factors for pancreatitis, commonly appear or worsen during this stage of a person's life.

Acute pancreatitis affects people of all ages, from young adults to the elderly, as seen by the average age of 42 years. This emphasises the importance of identifying and controlling risk factors and symptoms associated with pancreatitis in all age groups, as well as tailoring therapy tactics to the unique needs of each patient at different stages of life.

The study discovered that a high number of those diagnosed with acute pancreatitis were alcoholics, accounting for around 85.9% of the total. This observation is consistent with the findings of Savio G Barreto et al, who discovered that alcohol was the underlying cause in 92.6% of cases, while gallstones were found in 19%. Alcohol abuse is a major contributor to the occurrence of pancreatitis, but other factors such as gallstone disease, smoking, obesity, and genetic predispositions also have a substantial impact on the condition's pathophysiology. The observed distribution of pancreatitis severity among the 227 participants in my study is consistent with the incidence rates

reported in the sample Atlanta symposia. Specifically, 66% of the people had moderate pancreatitis, while 18% had severe pancreatitis. The alignment with existing incidence rates helps to validate my study findings and strengthens the dependability of the severity grading approach used. NLR can be used on a frequent basis to quickly assess the patient's health and establish a treatment strategy. The high prevalence of mild pancreatitis in my study emphasises the illness's common presentation, which is typically associated with milder symptoms and a favourable prognosis. On the other hand, the large number of patients with severe pancreatitis emphasises the importance of detecting, actively treating, and continuously monitoring this group of patients to avoid complications and improve outcomes. The death rate of 11% among the 227 participants in my study is a finding of concern that emphasises the gravity and potential implications of acute pancreatitis. Furthermore, the high percentage of people who develop acute necrotizing pancreatitis (5.7%) as a result of organ failure emphasises the critical importance of this disease and the necessity for early detection and intervention to minimise adverse effects.

Acute necrotizing pancreatitis is a severe form of the disease marked by extensive necrosis of pancreatic tissue with SIRS. It is associated with a high incidence of morbidity and mortality. The presence of organ failure, including respiratory, renal, and cardiovascular dysfunction, significantly increases the mortality risk in these individuals due to the systemic effects of pancreatic enzyme production, cytokine storm, and subsequent MODS.

The findings of this study show that a significant proportion of patients, precisely 56.38%, had blood amylase levels that were much higher than the normal range (>3 times the normal). This data suggests the existence of significant pancreatic inflammation and damage, which is consistent with the diagnosis of acute pancreatitis. The increase in serum amylase is a common biomarker in the diagnosis of pancreatitis because it shows injury to pancreatic acinar cells and the release of pancreatic enzymes into the bloodstream.

My study's principal findings show that patients with acute necrotizing pancreatitis had a much higher Neutrophil Lymphocyte ratio than those with mild attack of acute pancreatitis. Acute pancreatitis is a condition that generates inflammation and activates both innate and acquired immune responses. During systemic inflammation, neutrophils and platelets become activated and exert a regulated influence on the host's defences. However, in some cases, an exaggerated and extensive inflammatory response might result in a massive migration of cells to the

pancreas and the production of chemotactic and chemo attractant agents. This can lead to pancreatic damage and necrosis. The NLR was initially developed as a simple and measurable biomarker for assessing systemic inflammation in critically ill patients in the intensive care unit (ICU). The study assesses the efficacy of NLR as a prognostic marker for necrosis in people with acute pancreatitis, makes an important contribution to the field of pancreatic research. The strong correlation between NLR and CT results in people with acute necrotizing pancreatitis highlights NLR's potential efficacy as a non-invasive and easily accessible biomarker for predicting disease severity and prognosis. Furthermore, the statistical significance of NLR in predicting patient outcomes after acute pancreatitis demonstrates its potential as a prognostic diagnostic factor for assessing disease progression and directing therapeutic decisions. Increased NLR levels on days 0 and 2 predict a bad prognosis, resulting in more careful monitoring, intense supportive therapy, and the evaluation of ways to prevent difficulties and enhance patient outcomes.

While the variability of NLR over time may not follow a clear pattern, the persistent increase in NLR on specific days provides critical predictive insights into the likelihood of patient being discharged or suffering a major illness or death. Understanding how NLR evolves over time in relation to illness outcomes enhances the ability to anticipate future NLR outcomes and aids in risk assessment and treatment planning for acute pancreatitis patients.

The study's findings highlight the potential of NLR as an effective predictive tool in acute pancreatitis. It offers clinicians a simple and cost-effective way to assess risk and anticipate outcomes. In this difficult clinical circumstance, clinicians can use NLR's predictive powers to improve patient care and clinical results.

Conclusions

My study has shown that NLR is a reliable indicator of necrosis in acute pancreatitis. As a basic investigation, it incurs no additional fees for the patient. NLR has a high association with the prediction of necrosis of pancreas in patients of acute pancreatitis. Consistent daily observation will provide a dynamic picture of the host's immune response to pancreatitis, allowing for the prediction of necrosis of pancreas in the patient. The NLR evaluates the severity of acute pancreatitis on

multiple days (day 0, 1, 2) and predicts the patient's prognosis and outcome in terms of acute pancreatitis.

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