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Can Organ Failure and Infected Pancreatic Necrosis be Used to Forecast Mortality in Patients with Gallstone-Induced Pancreatitis?

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Abstract:-

- ***Objective***

Early identification of high-risk patients in a common emergency like acute gallstone-induced pancreatitis can be difficult. In patients with acute gallstone-induced pancreatitis, persistent organ failure is considered to be the most important cause of mortality. This study strives to understand the relationship between persistent organ failure with infected pancreatic necrosis and its relationship with mortality.

- ***Design***

We performed a prospective observational study of 219 patients diagnosed with acute gallstone-induced pancreatitis who were admitted to the Department of General Surgery, IGMC, Shimla. We tried to understand the relationship between the type of organ failure (single or multiorgan and systemic), infected pancreatic necrosis, and mortality.

- ***Results***

In total, 30 of 219 (13.69%) patients with acute GSP developed Persistent Organ Failure (of any type or combination) of whom 15 (6.8%) patients developed an infection of pancreatic necrosis. Mortality was seen in patients who had a concomitant infection of pancreatic necrosis and persistent organ failure (36.36% vs 0%, p=0.04).

- ***Conclusion***

In patients with infection of pancreatic necrosis, persistent organ failure is associated with increased mortality when compared to patients with absent persistent organ failure. As mortality was absent in patients without infected pancreatic necrosis, the impact on mortality is debatable.

Keywords:- *Infected Pancreatic Necrosis, Persistent Organ Failure, Acute Gall Stone Induced Pancreatitis, Mortality.*

I. INTRODUCTION

Acute pancreatitis is the most horrifying of all calamities that occur concerning the abdominal viscera. “The suddenness of its onset, the illimitable agony which accompanies it, and the mortality attendant upon it, all render it the most formidable of catastrophes” [1]. The incidence of acute pancreatitis has been growing worldwide. Acute GSP has an incidence of about 13 – 45 new cases per 100,000 per year of which 40-50% of cases are biliary in etiology. The estimated annual cost for admissions is a whooping 2.2$ billion each year with more than 300,000 inpatients admission and 20,000 deaths annually [2]. Gall disease is the most common cause of acute pancreatitis. In the early phase after the onset of pancreatitis, the release of inflammatory chemokines and cytokines during the systemic inflammatory response syndrome (SIRS) contributes to the development of organ dysfunction. Organ failure is a dynamic process that is not limited to the first week and may develop at any stage of the disease. In the early phase, conditions inducing pancreatitis and mediators of SIRS play an important role in the development of organ failure. Conversely, infected pancreatic necrosis or other infections such as pneumonia may also occur early in the disease course, thus it can be difficult to determine whether organ failure is caused by SIRS or sepsis.

Improved knowledge about the details of organ failure in acute pancreatitis will help to better estimate the prognosis of patients who suffer from organ failure, especially when end-of-life decisions need to be discussed after a prolonged period of organ failure. Furthermore, improved insight into the details and outcome of organ failure may provide a base for differential and new treatment strategies in severe acute pancreatitis.

A. Abbreviations and Acronyms

Abbreviations used in this paper: GSP, Gallstone Pancreatitis; IGMC, Indira Gandhi Medical College; IPN, Infected Pancreatic Necrosis; POF, Persistent Organ Failure; SIRS, Systemic Inflammatory Response Syndrome; MMS, Modified Marshall Score;

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II. METHODS

A. Patients and Study Design

This was a prospective observational study in IGMC, Shimla, HP, India. In summary, all patients diagnosed with acute GSP within the period from 1st April 2021 to 31st March 2022 were included in the present study without any bias. Patients were managed according to standard guidelines for the management of pancreatitis. Antibiotics were administered only if there was a suspected or proven infection. Prophylactic antibiotic therapy was not prescribed. Invasive interventions were generally performed only in case of suspected infected necrosis. The type of organ failure and infection of pancreatitis and its association with mortality was analyzed. Infective complications were diagnosed based on clinical, biochemical, and/or radiological investigation with image-guided culture/s reserved for a few selective cases without a diagnosis.

B. Data Collection

During the first three days of hospital admission, prospe ctive data collection was done on the demographics of the pat ients and the results of their lab tests. In addition, during the hospital stay, data regarding the onset, and type of organ failure (i.e., respiratory, cardiovascular, and renal failure) were registered. Age, sex, hospital stay length, organ failure (measured using MMS) at admission and after 48 hours, CTSI, and invasive procedures were also noted.

Table 1: Baseline characteristics at presentation

Baseline characteristics at presentation	
Hospital Stay, day, mean ± SD	8.04 ± 8.70
Sex, male/female	99/120
Age, years, mean ± SD	50.00 ± 15.22
Temperature, °C, mean ± SD	38.02 ± 0.61
Pulse Rate, beats per min, mean ± SD	80.00 ± 11.89
SBP, mmHg, mean ± SD	129.27 ± 23.56
DBP, mmHg, mean ± SD	72.36 ± 15.17
SpO2, %, mean ± SD	88.19 ± 5.18
RR, breaths per min, mean ± SD	20.04 ± 3.72
Hb, g/dL, mean ± SD	12.45 ± 2.39
HCT, %, mean ± SD	37.81 ± 7.15
TLC, thousand per mm^3, mean ± SD	12.04 ± 5.45
PLT, thousand per mm^3, mean ± SD	268.13 ± 100.53
BUN, mg/dL, mean ± SD	40.23 ± 17.46
Creatinine, mg/dL, mean ± SD	0.95 ± 0.60
S. Sodium, mmol/dL, mean ± SD	140.59 ± 6.24
S. Potassium, mmol/dL, mean ± SD	4.46 ± 0.87
S Chloride, mmol/dL, mean ± SD	95.22 ± 3.20
RBS, mg/dL, mean ± SD	127.70 ± 39.97
Total S. Bilirubin, mg/dL, mean ± SD	1.81 ± 1.16
Direct S. Bilirubin, mg/dL, mean ± SD	0.90 ± 0.58
Indirect S. Bilirubin, mg/dL, mean ± SD	0.64 ± 0.48
SGOT, U/L, mean ± SD	31.36 ± 12.04
SGPT, U/L, mean ± SD	30.68 ± 11.77
ALP, U/L, mean ± SD	130.61 ± 70.05
PT, U/L, mean ± SD	15.33 ± 3.21
INR, mean ± SD	0.94 ± 0.54
Amylase, IU/L, mean ± SD	1551.86 ± 805.46
Lipase, IU/L, mean ± SD	1732.76 ± 751.17

Contrast-enhanced CT (CECT) was routinely performed in case of clinical deterioration at the discretion of the treating physician. The presence of extra-pancreatic necrosis and the extent of parenchymal necrosis were based on CTSI.

C. Definitions

Acute GSP was diagnosed based on the Revised Atlanta Classification which required any two of the following three criteria:

- Typical upper abdominal pain homologous with acute pancreatitis.
- Serum lipase or amylase activity at least three times greater than the upper limit
- Characteristic radiological findings of acute pancreatitis [3]

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- **Organ Failure** was defined as failure of the respiratory, cardiovascular, or renal system.
- **Persistent Organ Failure (POF)** was defined as organ failure lasting for more than 48 hours.
- **Multiple Organ Failure** was defined as the failure of two or more two organ systems.
- **Necrotizing pancreatitis** was defined as either pancreatic parenchymal necrosis with or without extrapancreatic necrosis, or extrapancreatic necrosis alone**.**
- **Infection of Pancreatic Necrosis (IPN)** was defined as a positive culture of pancreatic or extrapancreatic necrotic tissue obtained by fine-needle aspiration or from the first intervention, or the presence of gas in the necrotic collections on CECT

D. Statistical analysis

Normal data are presented as mean ± SD or as median with IQR. Differences in continuous variables between patients with and without organ failure were tested with the Mann-Whitney U test. Proportions were compared using the χ^2 test or by linear-by-linear χ^2 association test in the case of ordinal categorical variables. Statistical significance was defined as $p < 0.05$.

Table 2: Relationship of characteristics with mortality

Characteristic	Mortality (%)	Survival (%)	Total
Age > 50	3 (3)	109(97)	112
Male Gender	2(2)	97(98)	99
Hospital Stay > 7 days	4(5)	69(95)	73
SIRS at presentation	4(2)	196(98)	200
Mild pancreatitis	0(0)	108(100)	108
Moderate pancreatitis	0(0)	75(100)	75
Severe Pancreatitis	4(11)	32(89)	36
Respiratory Failure	4(14)	24(86)	28
Cardiovascular Failure	0(0)	0(0)	0
Renal Failure	3(21)	11(79)	14
Persistent Organ Failure	4(13)	26(87)	30
Single Organ failure	1(6)	17(94)	18
Multiple Organ Failure	3(25)	9(75)	12
CTSI > 4	4(16)	21(84)	25
Necrotising Pancreatitis	4(16)	21(84)	25
IPN	4(27)	11(73)	15
POF with IPN	4(27)	11(73)	15
POF without IPN	0(0)	10(100)	10
IPN without POF	4(27)	11(73)	15

Table 3: Summary

Type of pancreatitis	No of patients (Percentage)
Mild	108 (49%)
< 7 days	79 (36%)
> 7 days	29 (13%)
Moderate	75 (34%)
Progressed	36 (16%)
Regressed	39 (18%)
Severe	36 (16%)
Edematous	11 (5%)
Necrotizing	25 (11%)
Sterile	10 (5%)
Infective	15 (7%)
Ecoli	10 (5%)
Klebsiella	4 (2%)
Others	1 (0.45%)

III. RESULTS

Organ failure occurred in 96 patients diagnosed with acute GSP of which 30 persisted after 48 hours. The baseline characteristics of the patients at the time of admission have been depicted in Table 1. Necrotizing pancreatitis was identified in 25 patients. Patients with organ failure had a higher incidence of pancreatic parenchymal necrosis, prolonged hospital stay, were older, had a higher percentage of pancreatic necrosis, and more often needed intervention. Overall mortality in 219 patients was 1.8% (n=4); of which only one patient had persistent organ failure. Out of 25 patients having necrotizing pancreatitis, 15 had an infection of pancreatic necrosis. All patients who died had infected pancreatic necrosis.

A. Type and combination of organ failure and impact on mortality

The prevalence and incidence of organ failure were high at the time of admission. 88 (91.66%) patients experienced respiratory failure, none of the patients experienced cardiovascular failure and 17 (7.76%) patients developed renal failure. Table 2 lists mortality rates in different subgroups of patients according to type and combination of organ failure. Transient organ failure occurred only in 96 of 219 patients. Of these 96 patients, 87 had single organ failure and 9 had multiple organ failure. Failure of the respiratory system occurred the most followed by renal failure. The mortality rate was 1.8% of which 75% of them had multiple organ failure and all of the had infected pancreatic necrosis. Further 30 patients had persistent organ failure, of which 18 had single organ failure and 12 had multiple organ failure.

B. Infection of pancreatic necrosis and its relation with mortality

Of the 30 patients who had organ failure, 15 had pancreatic necrosis infections. Patients with infected pancreatic necrosis without organ failure and those with sterile necrosis did not have any deaths.

In 15 patients with organ failure and infected pancreatic necrosis, the mortality was 36.36%. Table 3 depicts a summary of the study.

IV. DISCUSSION

This study was done to provide insight into the association between organ failure and infection of pancreatic necrosis with mortality.

Our study identified no association between organ failure and infected pancreatic necrosis. Previous studies show conflicting results concerning organ failure and its association with mortality. Organ failure is a dynamic process and regression/progression was observed even at 48 hours. The data collection included registration of type of failure from calculated MMS score, pancreatic necrosis from CECT, and its infection from single-time aspiration.

Previous studies also suggested that the influence of organ failure and infected pancreatic necrosis as mortality was similar and that the combination increased mortality. More recent studies have found that the influence of organ failure is stronger than that of the combination of organ failure and infected pancreatic necrosis and did not increase mortality in comparison with organ failure without infected pancreatic necrosis [4]. But we found that the combination of organ failure and mortality had a higher incidence than in infected pancreatic necrosis alone. No mortality was observed in patients with persistent organ failure alone. These differences may be explained by differences in study design and data collection. In our study, patients with acute GSP were prospectively included and data collection started on the day of primary admission after the onset of symptoms at the emergency department.

Other studies may have included patients that survived that first phase of the disease and inclusion was started after patients were transferred to pancreatic expert centers or inclusion started when patients were admitted to the ICU.

The determinant-based classification contains an additional category including patients with infected pancreatic necrosis and organ failure named ‘critical acute pancreatitis’. The clinical relevance of this category is based on studies suggesting that patients with infected pancreatic necrosis and organ failure are at excessive risk for mortality and our study supports this.

A limitation of our study is that the underlying cause of organ failure could not be specified. For example, organ failure caused by SIRS without documented infection and organ failure caused by sepsis may overlap in time and are difficult to distinguish from one another. This is a well-known limitation of studies regarding organ failure and infected necrosis.

Furthermore, pre-existing comorbidity plays an important role in determining outcomes in patients with necrotizing pancreatitis. Vulnerable patients with secure comorbidity may
develop organ failure faster compared with those without significant comorbidity. Another limitation of this study might be that we have used a modified Marshall Scoring System to define organ failure as proposed in the 2012 Revised Atlanta Classification. Endotracheal intubation for respiratory failure, use of vasopressors for persistent hypotension after fluid resuscitation, and renal replacement therapy for renal sufficiency are not incorporated in the modified Marshall Score. Patients receiving supportive therapies may show normal arterial oxygen measurements.

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CONTRIBUTORS

SKY drafted the manuscript in close collaboration with DKS coauthored the writing of the manuscript. The final text was peer-reviewed, modified, and approved by all authors.

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Competing interests None declared.
Patient consent Informed consent was taken from all participants.

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