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Association of Systemic Inflammatory Response syndrome with Serum Creatinine, Albumin, and C-Reactive Protein in Acute Pancreatitis Patients

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ABSTRACT

Background and aim: Acute pancreatitis (AP) is one of the leading causes of hospital admission from gastrointestinal diseases, with approximately 300,000 emergency department visits each year. Outcomes from acute pancreatitis are influenced by risk stratification, fluid and nutritional management, follow-up care, and risk-reduction strategies.
Objective: The current work aimed to assess the pattern and outcome of acute pancreatitis.
Patients and methods: A total of 70 patients with acute pancreatitis were enrolled. Those patients were subjected to history and clinical evaluation. All baseline laboratory and radiological data were recorded.
Results: Serum albumin was negatively correlated with the length of hospitalization. Severe inflammatory response syndrome was associated with higher C-reactive protein and serum albumin level, in the Contrast-enhanced CT (CECT) scan and systemic inflammatory response syndrome (SIRS) in the first 48 hours were significantly associated with severe inflammation and necrosis.
Conclusion: Acute pancreatitis is a challenging condition, which vary in severity and duration. Early diagnosis and severity classification have substantial impact on proper care. A more complicated disease is associated with the early onset of systemic inflammatory response syndrome.
Keywords: Acute pancreatitis, C-reactive protein, Severe inflammatory response syndrome.

INTRODUCTION

Acute pancreatitis (AP) is an inflammation of the pancreas that occurs suddenly. It might range from a minor ailment to a life-threatening illness. Abdominal discomfort and elevated pancreatic enzyme levels in the blood or urine are symptoms. Gallstones, alcohol misuse, and post-endoscopic retrograde cholangiopancreatography pancreatitis (ERCP) intervention are all recognised as risk factors [(1)]. For the duration of the disease, the Revised Atlanta classification classifies AP into mild, moderately severe, and severe acute pancreatitis [(2, 3)].

Hyperthermia (> 38.0°C) or hypothermia (36.0°C), tachycardia (> 90 beats/m), tachypnea (> 20 breaths/m), and WBCs > 12.000/mm^3 or 4.000/mm^3 with a score more than or equal to 2 are all signs of a severe inflammatory reaction [(4)]. Different severity grading systems, including SIRS, APACHE II, modified Glasgow score, and Ranson score, can be used to forecast the severity of the disease early [(5)].

Many laboratory biomarkers, such as, C-reactive protein (CRP), procalcitonin, and interleukin-6, can successfully predict the course of AP [(6)]. Severe pancreatitis is associated with marked inflammation and cell necrosis. Increased levels of cytokines or cytokine storm because of cellular injury is linked to severe inflammatory response syndrome (SIRS) and multi-organ failure [(7)]. In this study, we aimed to assess the pattern and outcome of AP in our locality.

PATIENTS AND METHODS

Study Design: This was cross-sectional study in which patients were recruited from El-Rajhi hospital with a diagnosis of AP. The study was conducted through the period from September 2019 to September 2020.
A total of 70 patients with acute pancreatitis were enrolled. Those patients were subjected to history and clinical evaluation. All baseline laboratory and radiological data were recorded.

Study Population:

Seventy AP patients were recruited for the study. The diagnosis of AP was based on two of the three following features: characteristic abdominal pain, serum amylase and/or lipase levels three times higher than the upper limit of normal and characteristic imaging findings [(8)].
Clinical Data Collection and Assessment: Patients' demographics (age, gender, length of hospital stays). Physical examination including vital signs, urine output, consciousness, GIT symptoms, and signs.

Laboratory tests: Renal and liver function tests, hematocrit level, differential white blood cells, electrolytes, blood PH, and CRP. All blood samples were withdrawn within the first day of admission with follow-up within 48 hours.
Imaging studies: Abdominal ultrasound to determine etiology and CECT scan.
Scores: APACHE-II, BISAP and SIRS were calculated within the first 48 hours. CT scan findings were classified according to the Balthazar computed tomography severity index (CTSI).

Ethical consent:

The study was approved by the Ethics Board of Assiut University and informed written consent was

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taken from each participant in the study. This work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis:

SPSS version 20 (Chicago, USA) was used to analyze the data. The variables were tested for normal distribution using Shapiro-Wilk test. Non-parametric data were expressed as mean ± standard deviation (SD) or number (percentage), whereas normally distributed data were expressed as mean ± SD or percentage. One-way ANOVA was used for comparison between parametric data. The Mann-Whitney U test was used for comparison between two groups, while Kruskal-Wallis H was done to compare the means of three groups. Chi-square (X^2) was used to determine significance for categorical variables. The correlation between variables was done by the Spearman correlation test. A difference was considered significant when the P-value was ≤ 0.05.

RESULTS

Demographic Data based on severity of AP (table 1):

The mean age of the group with SIRS was 53.28 ± 15.4 years and the majority (76%) of them were females. Also, group with no SIRS showed mean age of 42.67 ± 14 years and 83% of them were females with non-significant difference as shown in table (1).

Table (1): Demographic Data based on SIRS

Variables		SIRS		p value
		Yes (N=40)	**No (N=30)**	
Age (years) Mean ± SD		53.28 ± 15.4	42.67 ± 14	0.83
Gender	**Male**	13 (33%)	5 (16%)	0.134
	Female	27 (76%)	25 (83%)	

SIRS: severe inflammatory response syndrome; values are presented as mean, standard deviation (range), or number (%); a **P value** of 0.05 is considered significant.

Etiology, SIRS and CT data in subgroups of the patients (table 2):

Etiology was idiopathic 60.0%, biliary 12.5%, malignant obstruction 22.5%, and post-ERCP 5% in the SIRS group. While in the non-SIRS group, it was idiopathic 53.3%, biliary 30%, malignant obstruction 6.7%, and post-ERCP 10%. Regarding the CECT scan, 12.5% of the patients showed acute interstitial inflammation, 55% had acute interstitial inflammation with fluid collection, and 32.5% had necrotizing pancreatitis in the SIRS group.

In the non-SIRS group, 76.6% showed acute interstitial pancreatitis, 26.7% with a fluid collection, 6.7% showed only bulky pancreas, and none of them showed acute necrotizing pancreatitis.

Table (2): Etiology, and CT data in subgroups of the patients

Variables		SIRS		P value
		Yes ''No''=40	No ''No''=30	
		N	N	
Etiology	**Idiopathic ''No''=40**	24 60%	16 53.3%	
	Biliary ''No''=14	5 12.5%	9 30%	
	M. obstructive ''No= 11	9 22.5%	2 6.7%	
	post-ERCP ''No= 5	2 5%	3 10%	1.69
CECT	**Acute interstitial ''No''=25**	5 12.5%	20 66.6%	*< 0.001
	Acute interstitial with fluid collection ''No''=30	22 55%	8 26.7%	
	Acute necrotizing pancreatitis ''No''=13	13 32.5%	0 0%	
	Bulky pancreatitis ''No''=2	0 0%	2 6.7%	

CECT stands for contrast enhanced computed tomography, and **SIRS** stands for systemic inflammatory response syndrome. If the P value is less than 0.05, it is considered significant.

Hospital stays and severity parameters in subgroups of the patients (table 3):

As shown in table (3), regarding hospital stay (days), BISAP score, and CTSI, mean hospital stay in SIRS group was 9.4 days and 4 days in non-SIRS group with significant difference.

Table (3): Hospital stays and severity parameters in subgroups of the patients

Variables	SIRS		P value
	Yes ''N=40''	**No ''N=30''**	
Hospital stays (days)	9.48 ± 1.01	4 ± 0.94	<0.005*
BISAP	1.31±0.9	27±0.058	<0.001*
CTSI	5.35±2.6	2±0.47	<0.001*

BISAP: Bedside Index of Severity in Acute Pancreatitis**; CTSI:** CT severity index**; SIRS: severe inflammatory response syndrome**. Values are presented as mean, SD or number (%) *P value is significant if <0.05.

Laboratory data in subgroups of the patients (table 4):

Regarding total protein, HCT, total bilirubin, ALT, AST, creatinine, and urea, there was a significant difference concerning serum albumin, and creatinine. In terms of albumin, the SIRS group had a mean of 29.58 ± 0.9, while the non-SIRS group had a mean of 38.53 ±

1.5 g/l with significant elevation in the non-SIRS group. Serum creatinine in the SIRS group was 126.91 ± 15.86, and in the non-SIRS group, was 71.34± 4.23 with significant elevation in the SIRS group.

Table (4): Laboratory data in subgroups of the patients

Variables	SIRS		p value
	Yes ''N=40''	No ''N=30''	
Albumin (g/l)	29.588± 0.9	38.53 ± 1.5	<0.001*
Total protein (g/l)	59.638 ± 1.04	61.713± 1.46	0.238
HCT (%)	33.235 ± 0.98	33.71 ± 1.7	0.757
Total bilirubin (g/l)	17.98 ± 2.42	19.39± 3.7	0.744
ALT (IU/L)	121.15± 28.81	78.1± 15.6	0.497
AST (IU/L)	50.12 ± 7.3	57.08 ± 5.5	0.656
Creatinine (µmol/L)	126.91 ± 15.86	71.34± 4.23	*0.002
Urea (mg/dl)	12.85 ± 1.9	8.30 ± 1.5	0.234
ALP (IU/L)	209.22 ± 6.3	227.63 ± 55.1	0.801
INR	1.26±0.29	1.49±0.18	0.216

ALT: alanine transaminase**; AST:** aspartate aminotransferase**; HCT**: hematocrit; **SIRS: s**evere inflammatory response syndrome; **INR:** international normalized ratio *P value is significant if <0.05.

Comparison of CRP between SIRS and non- SIRS groups (table 5):

CRP was significantly higher in patients with acute pancreatitis who presented with early SIRS versus non-SIRS groups (207.3 ± 22.7, 106.7 ± 23.3 mg/l, respectively).

Table (5): Comparison of CRP between subgroups of the patients

	SIRS		P value
	Yes ''N=40''	No ''N=30''	
CRP (mg/L)	207.35± 22.7	106.7 ± 23.3	***0.003**

CRP: C-reactive protein; **SIRS: s**evere inflammatory response syndrome Values are presented as mean ± SE (range). P value is significant if <0.05.

Correlation between length of hospital stay and laboratory markers (Fig 1):

There was a negative correlation between serum albumin and duration of hospitalization (figure 1). Instead, there was a positive correlation between APACHE II score (figure 2), serum creatinine (figure 3), and length of hospitalization (r=0.619, P-value <0.001) and (r = 0.128, P-value 0.291) respectively.

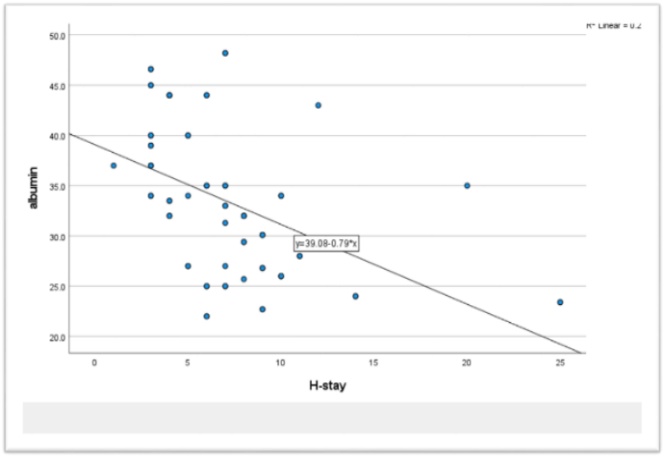

Figure (1): Correlation between serum albumin and hospital stay

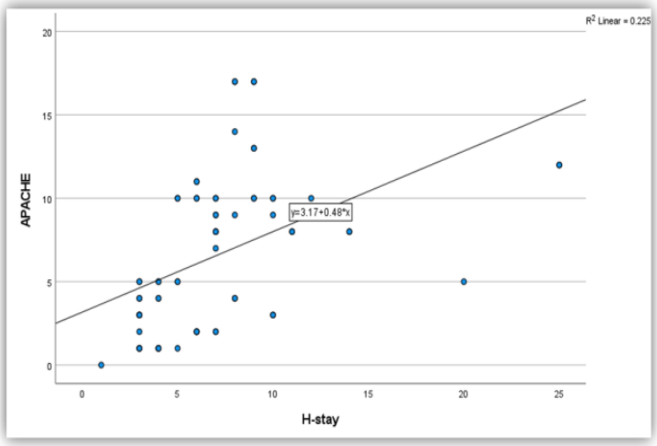

Figure (2): Correlation between APACHE II score and hospital stay.

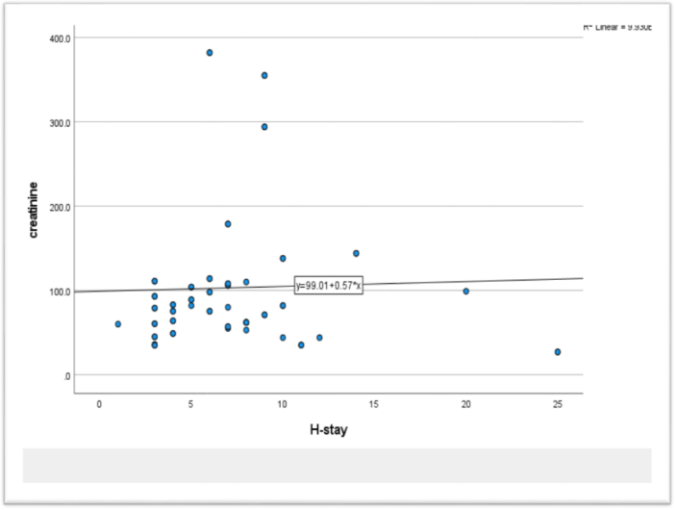

Figure (3): Correlation between serum creatinine and hospital stay

DISCUSSION

Acute pancreatitis (AP) is a pancreatic inflammatory condition characterised by quick onset of epigastric pain, increased serum amylase, and

distinctive contrast-enhanced CT scan abnormalities. According to many clinical and radiological characteristics, the Revised Atlanta classification system (2012) divided acute pancreatitis into mild, moderately severe, and severe acute pancreatitis across the course of the disease [2].

In terms of study group demographics, our study found a general predominance of females, but no significant difference between gender and severity criteria. **Hsiu *et al.*** [9] reported that gender is an important predictor of severity in patients with acute biliary pancreatitis. This contrasts with **Lankisch *et al.*** [10] who reported that gender is not an independent risk factor for the severity and outcome of acute pancreatitis.

In our study, idiopathic pancreatitis was the most predominant etiology, followed by biliary, post-ERCP, and lastly, malignant obstruction. Alcohol abuse is not prevalent in our locality. Generally, biliary, and alcoholic pancreatitis are the most frequent etiologies of acute pancreatitis. A systematic review of observational studies reported that the etiology of acute pancreatitis may differ geographically. For example, the US has idiopathic acute pancreatitis at the top of the list, whilst in Latin America, acute biliary pancreatitis was the most frequent [11]. According to **Alkareemy *et al.*** [12]**,** the most common etiology (56%) of acute pancreatitis patients were secondary to gall bladder stones, 26% were idiopathic, and 12% were ERCP. Idiopathic pancreatitis may be due to occult gall stones, dysfunction of the sphincter of Oddi, or cystic fibrosis in children or young adults [13]. **Xin *et al.*** [14] studied the etiology and clinical characteristics of acute pancreatitis in the elderly, he found that biliary and idiopathic causes were the most common and accounted for over than 90% of SAP in the elderly.

There was a non-significant difference between groups regarding total protein, HCT, total bilirubin, ALT, AST, and urea. However, there was a significant difference concerning albumin, serum creatinine, and APACHE score. The mean albumin level in SIRS groups was 29.5, whereas the mean albumin level in non-SIRS groups was 38.5 g/l with a P-value of 0.001*. Hypoalbuminemia in acute inflammatory conditions may be associated with previous malnutrition, comorbid conditions, or occur as a negative acute phase reactant. Albumin synthesis by the liver is downregulated at the expense of other inflammatory reactants. Either of these explanations, hypoalbuminemia at the onset of the disease has a strong predictive value for mortality and morbidity [15]. This may be explained by low healing capacity, more severe inflammation, and vascular extravasation. **Gibbs *et al.*** [16] concluded that low serum albumin levels can predict postoperative morbidity (sepsis and major infection) and mortality. Although marked fluid loss in acute pancreatitis through repeated vomiting and transudation of fluid and third space formation, increases hemoconcentration and HCT level, we found no significant variation between study groups regarding hematocrit level. **Remes-Troche *et al.*** [17] reported that neither HCT levels at admission nor hemoconcentration at 24 h were associated with the severity, necrosis, or organ failure of acute pancreatitis. As regards CTSI and APACHE II scores, we found a significant increase in both scores concerning the SIRS group. The APACHE II is a useful prognostic scoring system for predicting the severity of acute pancreatitis. **Kumar *et al.*** [18] reported that CTSI can predict severe acute pancreatitis, pancreatic necrosis, organ failure, and ICU admission. APACHE II was accurate in predicting severe acute pancreatitis and organ failure.

CRP, which is secreted by the liver in acute inflammatory and infectious diseases, has a rapid rise and rapid decline in response to disease onset and offset, respectively. Owing to its rapid response, its level is useful in the follow-up of the disease course. In our study, there was a significant difference in CRP level and SIRS criteria. Although many studies confirm that CRP is a good predictor for disease course, there are many drawbacks to the use of CRP level in inflammatory or infectious diseases owing to its low specificity. First, many drugs can falsely decrease the level of CRP like NSAIDs, statins, and magnesium supplements. Mild elevation of CRP can occur in other non-inflammatory conditions like insomnia, depression, and smoking. CRP cannot be synthesized properly in hepatic cell failure patients [19]. CRP is not a single molecule but rather native pentameric and modified monomeric molecules, each of which has a different biological role. The first can activate the complement system with activation of phagocytosis and apoptosis. The latter has proinflammatory and chemoattractant effects for inflammatory cells and chemokines. Only native CRP is available in commercial laboratories [20].

The main limitations of the current study were that the number of patients included in the study was small. Many patients seek medical advice in a private clinic before arrival at the hospital. This in turn delays the patient's presentation from the onset of the disease. As we included only patients within 48 hours of the onset of the disease and excluded those with delayed presentation, the sample size would be larger with higher power of the study if patients presented earlier. Idiopathic acute pancreatitis needs meticulous work up to delineate the cause and treat it, not only to prevent recurrent acute pancreatitis but also to prevent multiple complications, organ failure, and pancreatic necrosis associated with this etiology.

CONCLUSION

Acute pancreatitis frequently faces us in the clinical field. Early diagnosis and management of those patients with acute pancreatitis usually improves the outcome. Multicenter studies on large numbers of patients are warranted.

The informed consent was clear and indicated the purpose of the study, and they were free to participate or withdraw at any time without any obligation. Furthermore, participants' confidentiality and

anonymity were assured by assigning each participant a code number for the purpose of analysis only.

Conflicts of Interest: The authors declared that they had no conflicts of interest.

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Author contribution: The authors contributed equally to the study.

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