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C-reactive protein and Procalcitonin Levels in Acute Pancreatitis: A Study in A Tertiary Care Hospital in Bangladesh

Dr. Shanjidah Hoque[1*], Dr. Md. Rifat Hassan[2], Dr. Md. Naheen Rezuan Shehran Asif[3]

[1]Specialist, General Surgery, Evercare Hospital, Dhaka, Bangladesh
[2]Consultant, National ENT Institute, Tejgaon, Dhaka, Bangladesh
[3]MS ((Paediatric Surgery), Specialist, Evercare Hospital, Dhaka, Bangladesh

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***Corresponding author:** Dr. Shanjidah Hoque
Specialist, General Surgery, Evercare Hospital, Dhaka, Bangladesh, Email: dr.shanjidah@gmail.com

Abstract **Original Research Article**

Background: Acute pancreatitis is an inflammatory disease of highly variable severity, ranging from mild cases with low mortality to severe cases with high mortality. Numerous biomarkers have been studied as potential early predictors of the severity of this disease so that treatment can be optimally tailored to prevent complications. C-reactive protein and procalcitonin are the most promising single markers for assessment of major complications and prognosis. ***Aim of the Study:*** The aim of this study was to evaluate C-reactive protein and procalcitonin levels in acute pancreatitis. ***Methods:*** This was a prospective observational study. The study was conducted on 35 admitted patients with diagnosis of acute pancreatitis at BIRDEM General Hospital, Dhaka, Bangladesh from October 2016 to April 2017. Complete blood count, serum amylase, serum lipase, C-reactive protein and serum procalcitonin values were observed. Data were collected from history, clinical findings and investigations. Proper written consents were taken from all the participants before data collection. A predesigned questioner was used in data collection. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 23 program as per necessity. ***Results*:** Among the parameters of the patients, P values of CRP were 0.047 and procalcitonin (PCT) was 0.032, less than 0.05 which were statistically significant. These studies have shown that, serum procalcitonin (PCT) is a good marker for predicting severity and development of organ failure in acute pancreatitis and it is superior to serum C reactive protein. The negative predictive values and positive predictive value for the procalcitonin were higher (90% and 53% respectively) than the respective values for CRP (89% and 47% respectively). The values of PCT showed high sensitivity of 91% and specificity of 81% in predicting severe acute pancreatitis. The negative predictive value was high (90%) indicating that with a negative test result severe acute pancreatitis can be excluded with a high probability. ***Conclusion:*** C-reactive protein (CRP) and procalcitonin (PCT), can differentiate between mild and severe acute pancreatitis. As the predictor both C-reactive protein and procalcitonin level assessment can play an effective role in evaluating diseases condition related to appendicitis.

Keywords: C-reactive protein, Procalcitonin, Acute pancreatitis, Inflammation.

INTRODUCTION

Acute pancreatitis is an inflammatory disease of highly variable severity, ranging from mild cases with low mortality to severe cases with high mortality. The first description of the pancreas has been attributed to Herophilus of Chalkaidon about 300 B.C. The naming of this organ, pancreas (Greek: pan, all; kreas, flesh), was not recorded until 400 years later by Rufus of Ephesus (100 A.D.) [1]. The first classification system for acute pancreatitis was reported by Fitz in 1889 [2]. In 1901, Opie described the association of gallstones to acute pancreatitis [3]. Alcohol was firmly established as an important pathogenetic factor in 1917 [4]. More than 100 years ago, Chiari (1896) proposed that, intrapancreatic activation of zymogens leads to pancreatic auto-digestion and is a key factor in the pathogenesis of acute pancreatitis. The association of hyperamylasaemia with acute pancreatitis has been recognized since 1929. In the history of radiography, the pancreas was a hidden structure seen only indirectly through studies exploring the surrounding organs, such as barium examinations of the upper gastrointestinal tract. Sonography was the first method that permitted direct imaging of the pancreas [5]. Pancreatic imaging essentially developed further with the introduction of computed tomography (CT) [6]. The rationale for surgery in severe acute pancreatitis has evolved over the

last 50 years. Initially, total pancreatectomy was often recommended but it resulted in very high mortality rates [7]. The current thinking is that, the patients with infected pancreatic necrosis benefit from surgical debridement and drainage of the infected and devitalized tissue [8]. Further, surgery is often necessary if aggressive organ support in an intensive care unit seems inadequate for an acute pancreatitis patient with organ dysfunction. Procalcitonin (PCT) is a polypeptide consisting of 116 amino acids. It is the precursor protein of the hormone calcitonin. The half-life of PCT in the human body is 25-30 hours. No definitive role is known for PCT before its proteolytic conversion to calcitonin. It is released by hepatocytes and G-cells of the thyroid gland. Plasma procalcitonin (PCT) is a highly specific marker for the diagnosis of bacterial infection and sepsis and multiorgan failure [9]. Local complications of acute pancreatitis include pancreatic pseudocyst, acute peripancreatic fluid collection, necrotic collection, and walled-off necrosis [10]. Studies have demonstrated its role in the setting of sepsis and acute pancreatitis. PCT is produced exclusively in response to endotoxin or mediator released in bacterial infections. They are IL-1b, TNF & IL-6. It promptly rises within 6 to 12 hours upon stimulation. Plasma PCT values were found to correlate better than CRP levels and total leukocyte count with the total duration of hospitalization, ICU stay, as well as with the progression to severe acute pancreatitis. Plasma procalcitonin is an early and reliable prognostic indicator in acute pancreatitis [11].

METHODOLOGY

This was a prospective observational study. The study was conducted on 35 admitted patients with diagnosis of acute pancreatitis at BIRDEM General Hospital, Dhaka, Bangladesh during the period from October 2016 to April 2017. Complete blood count, serum amylase, serum lipase, C-reactive protein and serum procalcitonin values were observed. The whole intervention was conducted in accordance with the principles of human research specified in the Helsinki Declaration [12] and executed in compliance with currently applicable regulations and the provisions of the General Data Protection Regulation (GDPR) [13]. The study was approved by the ethical committee of the mentioned hospital. Proper written consents were taken from all the participants before data collection. As per the inclusion criteria of this study, only patients with acute pancreatitis were included. On the other hand, according to the exclusion criteria of this study, patient who were suffering from acute pancreatitis with multiple comorbidities like cerebrovascular diseases, CKD etcetera were excluded. Data were collected from history, clinical findings and investigations. All the demographic and clinical data of the participants were recorded. A predesigned questioner was used in data collection. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 23 program as per necessity.

RESULT

In this study, among total 35 participants, 54% were male whereas the rest 46% were female. So male participants were dominating in number and the male-female ratio was 1.2:1. Age distribution of all patients ranged from 28 to 76 years, where the youngest patient was of 28 years' and the eldest was of 76 years. Among total patients, 10 (29%) were within 46-55 years and 8 (23%) were within 56-65 years. The largest group patients were aged between 46 - 55 years and were comprised of 10 patients, which was 29% of the total study population. Complete blood count was done in all admitted patients. Heamoglobin were more than 10g/dl in 11 patients out of 14 patients with severe acute pancreatitis and 18 patients out of 21 patients with mild acute pancreatitis. Total white blood cells count showed leucocytosis in 27 patients out of 35 patients. Total white blood count was markedly elevated in a group of patients with severe pancreatitis as range between 8.1 and 38.3 comparatively higher than mild group where the range was 6.04-22.3. Differential count showed elevated neutrophil count in 11 patients out 14 patients with severe acute pancreatitis. The ranges of the neutrophil count were 58-79% in mild group of patients and 62-82% in the group of patients with severe acute pancreatitis. Lymhocytopenia developed in 6 patients out of 14 with severe acute pancreatitis. The range of lymphocyte count was 12-41% in patients with mild acute pancreatitis and 17-37% in the group of patients with severe acute pancreatitis. Monocyte, eosinophil and basophil count were found within the normal limit in both groups of patients. The baseline characteristics showed no significant difference between the two groups. In total 35 cases, serum amylase was significantly raised in 19 patients (54.28%) and serum lipase was elevated in 32 patients (91.4%). Raised lipase and amylase was found in 28 patients (80%), Raised lipase with normal amylase levels was found in 4 patients (11.4%). C-reactive protein has been showed to be a good severity predictor with a cut off level of 100 mg/l is used for distinguishing between the mild and the severe disease. Comparison with the C-reactive protein (CRP), procalcitonin (PCT) test had a sensitivity of 91% and specificity of 81% in severe acute pancreatitis. CRP was raised in 28 patients out of 35 patients and rest of patients had raised (PCT) in 11 out of 35 patients. Median value of CRP was 47.6 mg/L and PCT was 0.07 ng/ml. The ranges of CRP in total patients between 3.7-113.6 mg/L and ranges of PCT found between 0.035-8.4 ng/ml. The sensitivity of serum amylase was 62% and specificity was 42% with the cut of value of 400U/L. Positive predictive value was 45% and negative predictive value of serum amylase was 88%. With the cut-off of 240 U/l, the specificity of serum lipase to detect a patient with acute pancreatitis was 88%, but the sensitivity was 79%. Serum lipase determination is recommended as a confirmatory test. But lipase has poor predictive value. The negative predictive values and positive predictive value for the procalcitonin were higher (90% and 53%

respectively) than the respective values for CRP (89% and 47% respectively). The values of PCT showed high sensitivity of 91% and specificity of 81% in predicting severe acute pancreatitis. The negative predictive value was high (90%) indicating that with a negative test result severe acute pancreatitis can be excluded with a high probability.

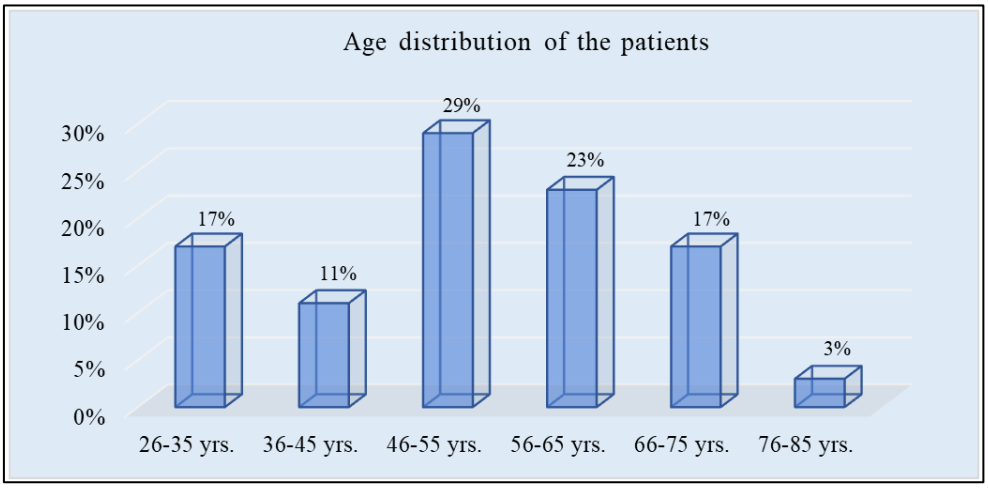

Figure 1: Column chart showed age wise distribution of study patients (N=35)

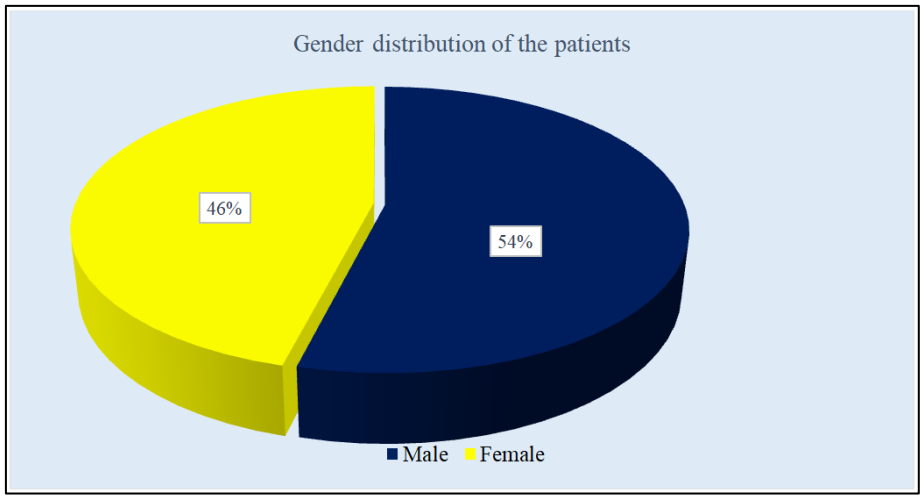

Figure 1I: Pie chart showed gender wise distribution of study patients (N=35)

Table 1: Distribution of study population by complete blood count of study patients (N=35)

Parameter	Patients Group	Frequency (n)	Median	Range	Standard Deviation (SD)
Haemoglobin(g/dl)	Mild	18	10.1	8-13.9	1.75
	Severe	11	11.4	8.9-16.6	
White Blood Cells					
Total Count(/L)	Mild	16	14	6.04-22.3	10.97
	Severe	11	21.6	8.1-38.2	
Differential count (%)					
Neutrophil	Mild	5	69	58-79	6
	Severe	11	75	62-82	
Lymphocyte	Mild	15	29	12-41	8
	Severe	6	27	17-37	
Monocyte	Mild	21	3.1	1.7-5.6	1.09
	Severe	14	3.1	1.8-6.6	
Eosinophil	Mild	21	2.2	0.03-5	1.52
	Severe	14	2.2	0.05-6	
Basophil	Mild	21	0.4	0.01-0.7	0.33
	Severe	14	0.4	0.03-0.9	

Table 2: Distribution of study population by serum amylase and serum lipase values of study patients (N=35)

Parameter	Frequency (n)	Median	Range	Standard Deviation (SD)
Serum amylase	19	514	34-1480	490.32
Serum lipase	32	785	13-1613	534.8

Table 3: Distribution of study population by serum PCT and C-reactive protein values of study patients (N=35)

	Frequency (n)	Median	Range	Standard Deviation (SD)
C-Reactive protein (mg/L)	28	47.6	101(3.7-113.6)	57.03
Procalcitonin (ng/ml)	11	0.0761	8.451(0.035-8.486)	2.13

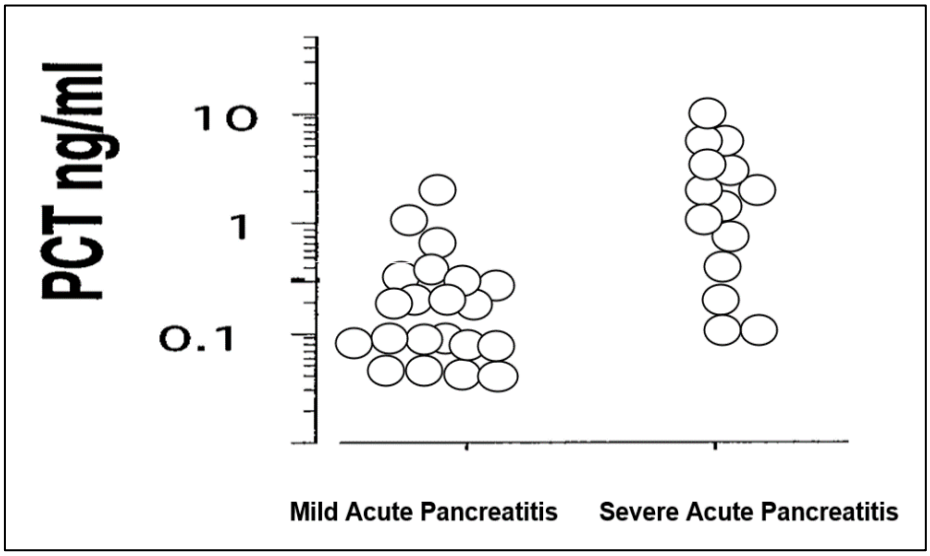

Figure III: Distribution of study population by C-reactive protein value (N=35)

Table 4: Comparison among the biochemical parameters

Variables	Cut of value	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Serum Amylase	400U/l	62	42	45.0	88.0
Serum Lipase	240 U/l	79	88	58.0	91.0
CRP	100 mg/L	78	69	47.0	89.0
PCT	2mg	91	81	53.0	90.0

DISCUSSION

The aim of this study was to evaluate C-reactive protein and procalcitonin levels in acute pancreatitis. In our study, we divided the patients into two groups; one group of patients had mild acute pancreatitis and another group of patients had severe acute pancreatitis. The classification system of acute pancreatitis proposed at the International Symposium on Acute Pancreatitis in Atlanta in 1992 for dividing acute pancreatitis into mild and severe disease is the internationally recognized guideline for clinical assessment of this condition and considers the disease as severe if local and/or systemic complications are present. Serum C-reactive protein is a proven predictor of severity for acute pancreatitis when serum level of over 150 mg/L is measured within 48 hours after the onset of symptoms [14]. However, very few studies have examined the power of CRP for predicting pancreatic necrosis [15]. It is important to emphasize that, PCT is not substitute for careful history and clinical examination of the individual patient. The cut off levels of PCT for predicting septic complications or overall prognosis are disease dependent and vary considerably among different inflammatory conditions [16]. Approximately 50%-70% of acute pancreatitis is caused by gallstones [17]. However, excessively high PCT concentrations were already present early after the onset of symptoms, which was days or even weeks before the infectious abdominal focus was ultimately diagnosed. Moreover, a similar course of PCT was observed in patients with severe acute pancreatitis. Our clinical observations are well in accordance with recent experimental studies suggesting a role for PCT in the prediction of severe acute pancreatitis [18]. A prospective international multi- center study by Bettina M *et al.*, [19] it was reported that; serum C-reactive protein is frequently used for assessing the severity of acute pancreatitis. Opinions about its relevance in the early prediction of severe acute pancreatitis are divided. On the other hand, Tenner *et al.*, reported that, CRP has no significance predictive role in assessing the severity of acute pancreatitis in the first 72 hours after admission [20]. Comparison with the C-reactive protein (CRP), the procalcitonin (PCT) test had a sensitivity of 91% and specificity of 81% in severe acute pancreatitis.

Another study by Kylanpaa-Back *et al.,* [8] also used PCT in the early detection of severe acute pancreatitis. They found that, the PCT was more accurate in predicting severe acute pancreatitis (sensitivity 92 % and specificity 84%) than CRP. A similar study by A. Olah *et al.,* [21] assessed the role of PCT in differentiating mild and severe acute pancreatitis and found that elevated levels of procalcitonin clearly suggest infections, while lower values do not exclude the possibility of local sepsis [21]. CRP was elevated in 28 patients and serum procalcitonin was elevated in 11 patients out of 35 patients. Cardoso *et al*., in their study emphasized the role of CRP in the early assessment of the severity of acute pancreatitis, especially in the case of a mild form of the disease [22]. C-reactive protein is an easily detectable marker that is frequently used to predict the clinical severity of acute pancreatitis, necrosis and mortality. CRP is able to differentiate between mild and severe acute pancreatitis with high precision, and to predict the development of severe acute pancreatitis even at 24 hours following hospital admission [23]. Patients with CRP levels >150 mg/l on admission to the emergency unit and on transfer to the intensive care unit have been shown to have significantly and independently worse outcomes that those with lower CRP levels. Although there is a 24-48 hours' latency period before CRP levels increase, which limits its utility as an early predictor of severity, CRP remains a useful predictor when levels have risen [24]. Other studies by Kylanpaa-Back *et al.,* [8] also used PCT in the early detection of severe acute pancreatitis and its negative predictive value was high (97%) and it detected in patient who developed subsequent organ failure. Early prediction of severity is an important goal in acute pancreatitis, in order to identify the 20% of patients who are likely to have a severe course. Such patients have an expected mortality of 15–20% and may benefit from early admission to high dependency or intensive care units [8].

Limitation of the Study

This was a single centered study with small sized samples. Moreover, the study was conducted at a very short period of time. So, the findings of this study may not reflect the exact scenario of the whole country.

CONCLUSION & RECOMMENDATION

C-reactive protein (CRP) and procalcitonin (PCT), can differentiate between mild and severe acute pancreatitis. As the predictor both C-reactive protein and procalcitonin level assessment can play an effective role in evaluating diseases condition related to appendicitis. For getting more specific results, we would like to recommend for conducting similar more studies in several places with larger sized samples.

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