International Journal of Advanced Multidisciplinary Research
ISSN: 2393-8870
www.ijarm.com
DOI: 10.22192/ijamr Volume 6, Issue 3-2019

Research Article

DOI: http://dx.doi.org/10.22192/ijamr.2019.06.03.003

Procalcitonin: A predictor for Acute Pancreatitis

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Abstract

Acute pancreatitis (AP) is not consistent in terms of its clinical presentation and severity. Various biochemical parameters, computerized tomography and certain scoring systems are used for this purpose and to determine the need for intensive care.

Methods: In these study patients of AP, who presented with the onset of symptoms by or before 48 hours were included. Blood samples were collected for the estimation of procalcitonin (PCT) on day of admission. Early identification of patients who develop severe acute pancreatitis would enable the selection of patients from early intensive management as severe acute pancreatitis is characterized by the development of systemic inflammation. This study was conducted to see whether procalcitonin, a marker of systemic inflammation, differentiated between patients with pancreatitis and other diseases.

Purpose of the present study carried out was to evaluate the relevance of procalcitonin as a predictor of disease**.**

Result: Of 115 patients of AP, 70% were male; mean age of presentation was 47 (ranged 18-90) years. Commonest risk factor for AP was gall stone disease (56.5%) followed by alcohol (19.1%). In 17.4 % of the patients, cause was idiopathic.

Conclusion: Serum PCT is potentially a simple and a reliable early biomarker in predicting the severity of AP; however require further research to confirm its accuracy.

Keywords

Procalcitonin;
Acute Pancreatitis,
C-reactive protein,
necrosis

Introduction

Acute pancreatitis (AP) is an essential medical condition and carries significant mortality and morbidity if not recognized and managed properly. AP is a disorder with devastating consequences.(1) Although most episodes are mild and self-limiting, about one fifth patient develops a severe attack that can be fatal.(2, 3) Early deaths in AP, within the first week, are due to multi-organ dysfunction syndrome (MODS) whereas late mortality is a consequence of local or systemic infections.(4) Therefore, early prediction of severe attacks is important, as it enables the timely administration of intensive supportive therapy and the early detection of complications.

Diagnosis is based on the presence of at least two of the following three features: Abdominal pain; increased pancreatic amylase, and/or lipase levels to ≥3 times the upper limit of normal; and imaging tests showing characteristic findings of acute pancreatitis.(5)

Several inflammatory markers are being used routinely in various hospitals in India to assess the prognosis of patients with acute pancreatitis. Among these are the total and differential leukocyte counts, erythrocyte sedimentation rate, and C-reactive protein (CRP) & Procalcitonin (PCT). Various scoring systems such as the Ranson's scores have also been used to stratify patients with acute pancreatitis.

Procalcitonin (PCT) is a calcitonin propeptide (molecular mass 13 kDa) made up of 116 amino acids. It is reported to increase early in severe infection and inflammation. (6, 7). Several studies on plasma PCT have demonstrated its role in the diagnosis of sepsis, prognosis of acute severe pancreatitis, and even as a prognostic marker following major surgery.(5, 6, 8-10). Beyond its value for the diagnosis of sepsis, PCT has also proved to be useful in monitoring the course and severity of the systemic inflammatory.

In general population, PCT is synthesized as the intracellular prohormone of calcitonin in the C cells of the thyroid gland and it is found in plasma as traces (~0.1 ng/ml). PCT was measured earlier by manual immunochemistry based method BRAHMS Kryptor assay; nowadays newer generation PCT assays are available like (Siemens and Roche), these are fully automated diagnostic analysers. In systemic infection or inflammatory state, PCT blood level increase within 3-6 hours, and continues till inflammatory process stays. Research says neuroendocrine cells of kidneys and lungs are possible source of PCT during state of sepsis and severe inflammation, the plasma concentration may ranges between 1 ng/ml and 1000 ng/ml; (11-14). Serum PCT is an ideal marker to diagnosis early sepsis and inflammatory condition due to its short halflife (approximately 24 hours) and thereby helps in monitoring disease progression (15). The major complications of acute pancreatitis are infected pancreatic necrosis, sepsis, and multi-organ failure and expect increase serum PCT levels; values above 0.5 ng/ml are considered abnormal (16). In this study we have investigated the appropriate cutoff values of serum PCT in different degree of severity of AP and assessed its validity as a prognostic marker.

Most of the studies on PCT have focused mainly on patients with sepsis in the ICU setting and on patients with acute pancreatitis. Information regarding the role of PCT as a marker of acute inflammation in our population is grossly inadequate. It is an established fact that ethnic and racial variations exist among various population groups even when it comes to interpretation of serological tests. Thus, Western data regarding these serological markers may not be applicable to our population. Hence, it is important to have data regarding the levels of various serological markers of inflammation in our own population so that they can be used routinely as diagnostic adjuncts, indicators for intervention, and prognostic markers for patients presenting with acute abdomen in our part of the world.

Initiating a step in this direction, this study aims to analyze the prognostic efficacy of plasma procalcitonin in patients presenting with acute pancreatitis and compare it with other prognostic indicators.

Methods

This is a prospective comparative study .115 patients who were clinically suspected to have AP were included in the study. The diagnosis of AP was based on acute upper abdominal pain radiating to back associated with a serum amylase level greater than three times the normal value or an elevated serum lipase level. Case that had the features suggestive of chronic pancreatitis, patients not giving written consent, patients with a history of trauma were excluded from the study. The cases were evaluated thoroughly in accordance with the standard practice, which included thorough history taking, general examination, systemic examination, laboratory investigations and imaging studies. Blood samples were sent for estimation of serum amylase level, serum lipase level, serum electrolytes, creatinine, blood urea nitrogen, liver function test, arterial blood gas analysis, complete haemogram, coagulation profile, lipid profile, CRP levels, and blood or urine culture in febrile patients. These investigations were repeated in accordance to the need and as per hospital protocols after admission. Serum PCT was measured within first 24 h after admission. Appropriate data were recorded to permit calculation of the Ranson's scores. Ranson's score was calculated at and 48 hrs after admission. Patients with Ranson's score ≥ 3 were considered severe form of AP.

Patients were considered to have alcoholic pancreatitis if they consumed alcohol on a regular basis, or had alcohol binge prior to the onset of symptoms. Patients were diagnosed as a case of gallstone pancreatitis if gallstones are found in USG or with the previous history of gallstones. Rests of all were labeled as idiopathic pancreatitis. All the patients were admitted and managed with adequate intravenous fluids,

analgesics, and prophylactic antibiotic therapy if indicated. Patients with vomiting were kept nil per oral soon after admission and nasogastric aspiration was done. Oral feeding was permitted as early as possible.

Results

Among 115 patients 70 (70%) were males and 45 (45%) were females. In our study on analyzing the etiology, we observed that the etiologies of AP included gallstone (56.5%), alcoholic (19.1%), idiopathic (17.4%), drug (4.3%), Hypercalcemia (0.9%), hypertriglyceridemia (0.9%) and post-ERCP (0.9%) shown in Table 1.

Table 1 showing sex, various age group, etiology and clinical presentation

Patient characteristics	Number of cases	Percentage (%)
sex		
Male	70	60.9
Female	45	39.1
Age group(years)		
<20	0	0
20-39	43	37.4
40-59	44	38.3
60-70 and above	28	24.3
Etiology		
Biliary	65	56.5
Alcoholic	22	19.1
Idiopathic	20	17.4
Drug	5	4.3
Hypercalcemia	1	0.9
Hypertriglycedemia	1	0.9
Post- ERCP	1	0.9
Clinical presentation		
Pain radiating to back	27	23
Non radiating pain	84	73
Vomiting	71	61.7
Abdomen tenderness	55	47.5
Guarding	26	22.6
illeus	23	20

Discussion

Acute pancreatitis (AP), defined as the acute nonbacterial inflammatory condition of the pancreas, is derived from the early activation of digestive enzymes found inside the acinar cells, with variable compromise of the gland itself, nearby tissues, and other organs.

AP is a major surgical challenge and assessment of severity of AP is important for early identification of risk of complications and mortality and also in improving outcome.(17) The ideal predictor of the severity of AP is described as being simple, highly sensitive, highly specific, safe, reproducible and cheap and can be rapidly performed.(18)The nature and purpose of this research work was to evaluate the ability of the serum PCT as a single biochemical marker in predicting the severe acute pancreatitis (SAP). In 2000 Toh et al. conducted a prospective study and they found AP was more common in males.(19) Similarly, in our study there was male predominance. Toouli et al. found AP is more common in the age group 40-60 years, however in our study it was 40-50 years. (20)

Forsmark et al. mentioned in their review article that gallstones (40%) was most common cause of AP followed by alcohol (30%).(21) In our study also, gallstones (56.5%) was found the commonest cause of AP followed by alcohol (19.1%) and idiopathic (17.4%).

The present study was intended to ascertain the best cut-off values of PCT to stratify severity in AP and assess efficacy of various severity indices in predicting their end result. Severity is defined by the emergence of local complications and/or distant organ dysfunction: 10% to 20% of patients meet a SAP attack, associated with both local and systemic complications, resulting a prolonged hospital stay and high morbidity and mortality (22). Early diagnosis and assessment of disease severity at admission is central to appropriate clinical management. Prognostic criteria can be classified into four categories: clinical signs, biochemical indicators, multi-factor grading systems and imaging procedures. Within 48h of admission, clinical assessment is as accurate, if not better than any other means of assessing the prognosis of acute pancreatitis. Several multi-factor grading systems have been devised to identify patients at higher risk. Various biochemical assays, quantify the products released by the pancreas as consequence of inflammatory reaction, have been developed to identify severe disease and/or pancreatic necrosis before the occurrence of multiple organ dysfunctions. The scoring systems of patients with AP helps in many ways, clinicians are aware of potential severity of disease and can be used comparison tool to assess effectiveness of new treatment within and between patient series. Sadly, at the moment the scoring systems are often insufficient to predict severity and recognize early organ failure (23-25). Therefore, a reliable scoring system or single biomarkers that adequately characterize the severity of AP is warranted. In this study; PCT was used a simple single biomarker topredict the severity of AP.

The most important step in the diagnosis and treatment of acute pancreatitis is differentiation between severe and mild cases. Scoring systems are employed to determine the severity of acute pancreatitis as soon as possible and to identify any need for intensive care. To determine the Ranson's score, which is used to establish the severity of pancreatitis, 11 parameters are evaluated and the waiting time is 48 h. The APACHE II scoring system, on the other hand, is a practical method that includes the patient's age and chronic disease state as well as 12 physiological values. (21) Thus, there is a recognized need for a method for determining the severity of acute pancreatitis which can be applied daily, can easily be evaluated, which is practical and has a high rate of specificity and accuracy. PCT is a glycoprotein that increases selectively in cases of bacterial inflammation, sepsis, and multi-organ failure. In normal healthy individuals, PCT is synthesized as the intracellular prohormone of calcitonin in the C-cells of the thyroid gland, and it is found at picogram levels in the plasma (~0.05 ng/ml). In cases of severe inflammations and sepsis, however, the plasma concentration ranges between 1 ng/ml and 1000 ng/ml; possible sources of this PCT are neuroendocrine cells in the lungs and kidneys.(19,21) A large number of studies have assessed the role of plasma PCT and compared it to other inflammatory markers in predicting the severity of pancreatitis and the development of infected necrosis.(26-32)These studies have shown that plasma PCT is a good marker for predicting severity and development of organ failure in acute pancreatitis and as well as predicting the development of infected pancreatic necrosis.

A prospective international multicenter study by Rau *et al*. (33) assessed the role of plasma PCT in the development of pancreatic infections and overall prognosis of severe acute pancreatitis. In their study, they monitored both plasma PCT and CRP values routinely and concluded that monitoring of plasma PCT allows early and reliable assessment of clinically relevant infections and overall prognosis in acute pancreatitis and thereby contributed improved stratification of patients at risk to develop major complications.

In a prospective study by Kim *et al*.(34) assessed the role of PCT in early prediction severe acute pancreatitis and concluded that PCT levels of 0.5 ng/ml has only sensitivity and specificity of 87% and 24%, respectively, whereas Ranson's score of ≥3 has sensitivity and specificity of 92% and 97%, respectively.

Conclusion

Certain predictive methods, such as the Ranson's score, CTSI score have been established as important methods for assessing the severity of AP but these multifactorial scoring systems are complex and hard to use in clinical bases. Serum PCT is an early marker of systemic bacterial infection, sepsis, and multi-organ failure. In this study, it was found that increased serum levels of PCT serve as a promising simple biomarker of prediction of severity of AP with better accuracy when compared with other scoring systems. Therefore, serum PCT as an index marker to assess the severity of AP can be used instead of complex scoring systems like Ranson's and BCTSI and CRP.

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Quick Response Code

DOI:10.22192/ijamr.2019.06.03.003

How to cite this article:
Sanjay Kisanrao Khopade, Satish Jain. (2019). Procalcitonin: A predictor for Acute Pancreatitis. Int. J. Adv. Multidiscip. Res. 6(3): 15-20.
DOI: http://dx.doi.org/10.22192/ijamr.2019.06.03.003