Evaluation of Procalcitonin as an Early Prognostic Marker in Acute Pancreatitis

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ABSTRACT

BACKGROUND

Acute Pancreatitis is usually a mild disease with minimal organ dysfunction. Sometime it can have severe complications and high mortality despite treatment. There is a need to identify patients at risk for complications so as to provide an early effective management. Procalcitonin, an inflammatory biomarker increases in acute pancreatitis with complications. So, we studied procalcitonin serum levels in acute pancreatitis patients to see if it can be used as an early predictor of development of complications.

METHODS

This was a prospective observational study, carried out at our tertiary care teaching hospital, north INDIA. A total of 60 cases were included in this study as per the inclusion criteria. Serum procalcitonin of ≥0.5 ng/ml was taken as significant.

RESULTS

Serum procalcitonin (PCT) was found to be non-significant in 61.6% (37 out of 60) patients, out of these, none had any complication, antibiotics use, low CT Severity Index (CTSI) score, early recovery and no death. Serum procalcitonin (PCT) was significant in 38.3% (23 out of 60) patients. CTSI score (>5) in 19 of these patients. Hypotension and respiratory failure were seen in 20 and 21 patients respectively with a significant p value of 0.001. Antibiotic use was observed in all the 23 patients in this group (p value 0.05). Duration of hospital stay was longer (more than mean 7.08±4.018 days) with significant p value of 0.005. Four participants died due to the complications related to acute severe pancreatitis. Mean value of PCT in participants who died was 4.2 ± 3.47 ng/ml with p value of 0.005

CONCLUSIONS

Serum procalcitonin level in acute pancreatitis had good correlation with development of complications of cardiovascular, respiratory system, high CT score, and longer duration of hospital stay, antibiotic use and death. Hence procalcitonin can be used to predict complication at an early stage of acute pancreatitis.

KEYWORDS

Acute Pancreatitis, Prognostic Marker, Procalcitonin

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BACKGROUND

Acute pancreatitis is an acute inflammation of the pancreas. It is one of the most common diseases of the gastrointestinal tract, leading to tremendous emotional, physical, and financial human burden. It can have severe complications and high mortality despite treatment. Acute pancreatitis is classified into mild, moderate and severe on the basis of Atlanta classification. Mild cases of acute pancreatitis do not have any complication or organ failure and are often successfully treated with conservative measures, while severe cases have persistent organ failure, do require admission to the intensive care unit, antibiotics use or even surgery to deal with the complications.

Alcohol and gallstones are the most common causes of acute pancreatitis, other causes include hypertriglyceridemia, hypercalcemia, post-endoscopic retrograde cholangio-pancreatography (ERCP) and drug-induced pancreatitis. Microlithiasis is also fairly common. Patients with recurrent acute pancreatitis and should be evaluated further especially using endoscopic ultrasound (EUS).[1] Among toxin-induced pancreatitis, smoking is being increasingly incriminated as an important causative factor.[2,3]

Mild and moderate cases of acute pancreatitis usually present with minimal organ dysfunction but 15-20% of all cases however present as severe acute pancreatitis.[4] In every patient of acute pancreatitis, early assessment of the patient can lead to an early and accurate prediction of the severity of the disease. There are several biochemical parameters, contrast enhanced computed tomography (CECT) and many other multiple clinico-biochemical scores for assessing the severity of acute pancreatitis.[5-7] Most of the severity scoring systems like Ranson, Glasgow, APACHE II,are very cumbersome to do and typically require 48 hours to become accurate, and when the score demonstrates severity, the patient's condition and disease will become obvious regardless of the score.[8,5-6] Even the new scoring systems, such as the BISAP, had not shown to be any more accurate than the other scoring systems.[7,9-10] So in general, acute pancreatitis-specific scoring systems have a limited value, as they provide very little additional information to the clinician in the evaluation of patients and may delay appropriate management.[11] There are also other various laboratory parameters such as the haematocrit and blood urea nitrogen (BUN) which can assist clinicians to assess severity but in real no laboratory test is consistently accurate to predict the severity in patients of acute pancreatitis.[8,12-16] Even the acute-phase reactant C-reactive protein (CRP), the most widely studied inflammatory marker in acute pancreatitis, is not practical as it takes 72 hours to become accurate.[17] CT or MRI imaging are also not much reliable early in the course of disease to determine severity of acute pancreatitis, as necrosis is usually not present at time of onset and it usually develop after 48-72 hr.[18] Due to this clinicians have been largely unable to predict who with acute pancreatitis will develop severe disease.

Thus, in the absence of any available test to determine severity earlier, close examination of vitals, general condition along with lab parameters is crucial to assess early fluid losses, hypovolemic shock and symptoms suggestive of organ dysfunction. Thus there is need of an ideal prognostic method/test which should be simple, inexpensive, routinely available and highly accurate and can be used to predict severity in acute pancreatitis earlier. Procalcitonin an inflammatory biomarker has shown promising results as an early marker of development of complication in sepsis and inflammation.

Procalcitonin is a peptide precursor of the hormone calcitonin, the latter being involved with calcium homeostasis. It is composed of 116 amino acid and is produced by para follicular (C cells) of the thyroid and by the neuroendocrine cells of the lungs and the intestine. The level of Procalcitonin in the blood stream of healthy individuals is below the limit of detection (0.1 µg/L) of clinical assays. Bacterial toxins, such as endotoxin and cytokines including tumour necrosis factor (TNF)-alpha, interleukin-1-beta, and interleukin-6 are known trigger factors for synthesis of procalcitonin in case of inflammation caused by bacterial infection but it can also rise in non-infectious cause of inflammation like trauma, shock, burn and surgery.[19] It does not rise significantly with viral or non-infectious inflammations. A severe infection with an associated systemic response the blood levels of Procalcitonin may rise to 100 µg/L. In serum, Procalcitonin has a half-life of 25 to 30 hours.[20] As Procalcitonin increases in acute pancreatitis and in other inflammatory situations like bacterial sepsis, multiorgan dysfunction and acute pancreatic necrosis,[21,22-24] we studied procalcitonin level during early course of acute pancreatitis subjects as early predictor of the development of complications.

We wanted to evaluate procalcitonin (PCT) as an early predictor of severity in acute pancreatitis by correlating the PCT value with CT severity score, complications, use of antibiotics, duration of hospital stay, recurrence, and death.

METHODS

This was a prospective observational hospital based study conducted at Government Medical College and Hospital, Sector 32, Chandigarh India. Patient who were diagnosed as case of acute pancreatitis on basis of diagnostic criteria as per Atlanta classification 2013 guidelines[25] were included. Total of 60 cases were included in this study.

Inclusion Criteria

1) Age more than 18 years.
2) Diagnosed cases of acute pancreatitis on basis of Atlanta 2013 guidelines.
3) Those who gave consent for study.

Exclusion Criteria

1) Co-infections like hepatitis B, C, and HIV infection.
2) Presence of any wound or septic foci which can lead to increase in serum PCT level.
3) Acute pancreatitis due to any intervention like surgery or ERCP.
4) Traumatic pancreatitis.

Methodology

At the time of admission to medicine emergency/ward/ medicine ICU patients those who met the inclusion criteria and willing for study were enrolled. These subjects were explained about the study and its purpose through the Patient Information Performa. After enrolment, patient's demographic data was taken along with a comprehensive history. A complete physical examination was performed and blood samples for procalcitonin with other relevant investigations (complete blood count, serum electrolytes, renal function test, liver function test, amylase, lipase, coagulogram, blood culture) were done. Procalcitonin was estimated by Using Chemiluminescence Immunoassay on ADIVA CENTAUR. Plasma level of procalcitonin in healthy individuals are quite low (0.1 ng/ml), cut-off for the diagnosis of sepsis, plasma level of ≥0.5 ng/ml was interpreted as abnormal. Statistical analysis was done using the latest SPSS software. All categorical variable were compared by using Chi-square and fisher's exact test. The predictive power of indicators was additionally demonstrated by calculating sensitivity, specificity, PPV (positive predictive value), and NPV (negative predictive value) of the sample in the usual way, using the optimal cut-off. For all statistical analysis, P <0.05 was considered significant.

RESULTS

The mean age of participants (including both male and female) in our study was 38.5±11.83 years with range of 22-65 years. There were 41 males (68.3%) and 19 females (31.6%) participants in the present study. Of the 60 patients, alcohol was a precipitating factor for acute pancreatitis in 34 patients (56.6%), consisting of 33 males (97%) and 1 female (2.9%). Gallstone was etiological factor in 26 patients (43.3%), of which 18 were females (69.2%) and 8 were male (30.7%). Serum Procalcitonin was measured in all 60 patients after establishing the diagnosis of acute pancreatitis within 48 hours of admission, value above/equal to 0.5 ng/ml was taken as significant. Mean value calculated was found to be 0.98 ± 1.738 ng/ml in 60 patients. CT severity scoring was done in all the subjects, our study found severity score of >5 in 21 patients out of which 19 had procalcitonin level above the cut off limit as shown in table 1.

7 patients had hypotension out of 23 with increased procalcitonin level as against none from 37 with normal procalcitonin, with mean procalcitonin of 2.3±2.4ng/ml (p value 0.001). Mean value of procalcitonin in patients with CNS complication was 1.5 with standard deviation of 0.96ng/ml and p value was 0.634. Respiratory complications had mean procalcitonin value of 2.3 with standard deviation of 0.26 ng/ml with significant p value i.e. 0.001. Antibiotics were used in 38.3% of the total study population, and all 23 patient with increase procalcitonin were on antibiotics, mean value of procalcitonin was 1.9 ± 0.38 ng/ml with p value of 0.05. Out of 60 none had any surgical procedure for acute pancreatitis or its complications. In our study 10 out of 23 patients with increased procalcitonin levels got re-admitted as against 4 out of 37 with normal procalcitonin as depicted in table 1. Mean value of PCT in re-admitted patient was 1.62 ng/ml with standard deviation of 0.78 ng/ml with p value 0.112. Of total 60 subjects 4 died, all had increased procalcitonin at admission, mean value of PCT in participants who died was 4.2 ± 3.47 ng/ml with p value of 0.005 (Figure 2).

The collective correlation of different parameters between two group of participant with raised procalcitonin and normal, showed that systemic complications, re-admissions, prolong hospital stay and death is more in raised Procalcitonin group as shown in figure 1.

Procalcitonin	< 0.5 ng/ml	≥0.5 ng/ml
Total Participants	37	23
Mean Procalcitonin	0.38 ± 0.66 ng/ml	1.9 ± 2.4 ng/ml
CTSI (>5)	2	19
Complications		
CVS	0	7
Respiratory	0	8
CVS + RS	0	11
CVS + RS + CNS	0	2
Duration of hospital stay (days)	13	19
Antibiotic use	0	23
Surgery	0	0
Recovery	37	19
Re-admission	4	10
Death	0	4

Table 1. Collective Correlation Data of Patients between Normal vs. Raised PCT with Different Clinical/Outcome Parameters

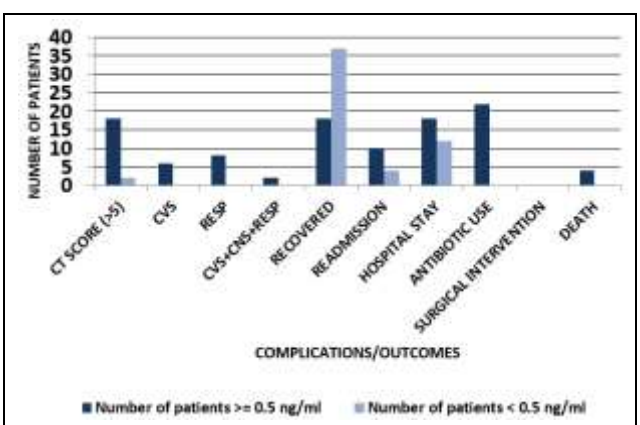

Figure 1. Number of Patients with Complications/Outcome

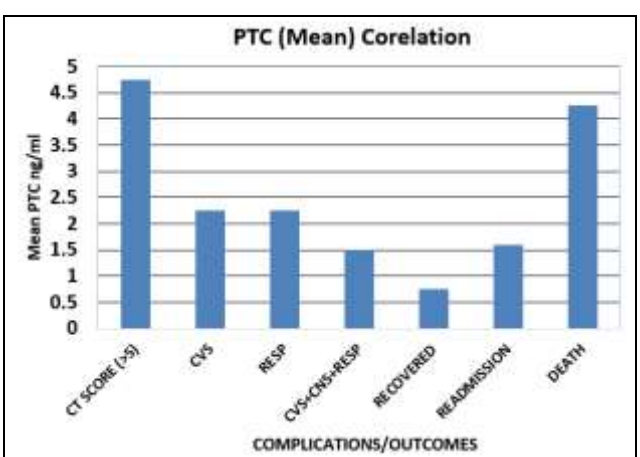

Figure 2. Mean PTC Correlation with Complications/Outcome

DISCUSSION

In our study acute pancreatitis was more commonly seen in men associated with alcoholism, followed by gall stones in females, similar to a study conducted at IPGMER, Kolkata Eastern India from January 2014 to January 2017 in 234 patients.[26] Procalcitonin in our study was found to be high in patients of severe acute pancreatitis and the same observation were made at two different study done at Poland by Kolber et al[27] and at Finland by Back et al[28] receptively.

Mean value of CTSI score was 4.7±3.0 (ranges from 1-10). 21 patients had CTSI score more than 5 especially in those subjects with raised procalcitonin. Study conducted in Department of Radiology, Division of Abdominal imaging and intervention, Brigham and Women's hospital Harvard Medical School, Boston in year 2010 on about 397 patients of acute of pancreatitis, concluded that CTSI score is more accurate in diagnosing patient clinically of severe disease and better correlate with need of early intervention or pancreatic infection.[29]

A Chinese study by Zhu et al conducted on 74 patients of acute pancreatitis and a total of 47 patients (63.5%) showed organ failure, 20 patients (27.0%) multiple organ failure, whereas 27 patients (36.5%) with dysfunction of a single organ system. Respiratory failure was the most common organ dysfunction (23.0%) (p=0.001) among single organ failures.[30] Similar results were observed in our study. In our study antibiotic use was observed only in patients with procalcitonin more than 0.5 ng/ml similar to a Chinese study by Rong et al,[31] but we didn't measure PCT daily to stop or change antibiotics. In our study duration or change of antibiotic were done on basis of clinical and lab parameters. Surgical procedure was not done on any patient in our study. In present study therefore, a positive correlation was observed of increased serum PCT with CTSI score, systemic complications, increase duration of hospital stay, antibiotic use, recurrence of symptoms and death.

Study done in Germany on 55 patients with acute pancreatitis, found high median concentration of PCT ranges from 1.7 to 3.1 ng/ml in patients of infected necrosis (p<0.001)and in those who had organ failure median PCT was 28.2 ng/ml.[32] These finding were consistent with our study.

CONCLUSIONS

From above study, we have observed that in a population with the mean age of 38.5±11.83 years, who developed acute pancreatitis had alcohol as the most common aetiology among males followed by gall stones in females. Procalcitonin was found to be raised (>0.5 ng/ml) in patients with, high CTSI score (5 or more), systemic complications (respiratory more than cardiovascular), longer duration of stay in hospital, re-admission due to recurrence of symptoms and high mortality. In this study, Procalcitonin has shown promising results as an early marker of development of complications. It is a simple, inexpensive, routinely available and highly accurate test. So, it can be used as an early predictor of severity in acute pancreatitis to reduce mortality by early intervention.

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