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STUDY OF SERUM PROCALCITONIN AS A PROGNOSTIC MARKER IN ACUTE PANCREATITIS

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ABSTRACT

Background: One of the main factors influencing the severity of AP (Acute Pancreatitis) in its latter stages is IPN (Infected Pancreatic Necrosis). Finding the best predictors of this severity variable is crucial because IPN is the primary cause of death in AP. Early triage of patients in need of transfer to a referral centre, ICU (Intensive Care Unit) treatment, and/or particular therapies is made possible by an accurate indicator of IPN. We looked at the procalcitonin level as an early indicator of the emergence of problems during the early stages of acute pancreatitis.

Methods: This study was conducted over a period of 18 months involving 130 patients diagnosed with acute pancreatitis. CRP, serum procalcitonin levels and CECT results were analysed.

Results: Patients who had respiratory complications had a serum procalcitonin range from 16.5 to 22.7 ng/dl. Among patients who had renal complications, serum procalcitonin was 15.1 to 18.3 ng/dl. Similarly, patients with severe pancreatitis who developed MODS had a very high range of serum procalcitonin, 16-44.1 and 37.7-112.6 ng/dl, respectively. CRP level did not increase in uncomplicated pancreatitis after two weeks of admission, whereas in MODS and severe pancreatitis it significantly increased. Both CRP and serum procalcitonin levels increased with an increase in the CT severity index.

Conclusion: Our study shows that PCT closely correlates with both infected necrosis and the severity of associated systemic complications. PCT could be a potential independent new indicator for selecting patients with acute pancreatitis at risk of developing infectious necrosis.

Keywords: Procalcitonin, Infected Pancreatic Necrosis, Acute Pancreatitis.

INTRODUCTION

The presence and amount of necrosis greatly raises the incidence of infection up to 80% and is linked to substantial mortality and morbidity, even though the total infection rate in acute pancreatitis does not surpass 10%. Patients with acute pancreatitis and sepsis in the intensive care unit have been the primary subjects of the majority of PCT research. There is a glaring lack of information about PCT's function as a marker of acute inflammation in our population. Even in the interpretation of serological

tests, it is well known that there are racial and ethnic differences among different population groupings. Our population may not be able to use Western data on certain serological markers. In order for them to be regularly used as diagnostic adjuncts, intervention indicators, and prognostic markers for patients presenting with acute abdomen in our region of the world, it is crucial to have data on the levels of different serological markers of inflammation in our own population. This study sought to examine plasma procalcitonin levels in patients with acute pancreatitis and those experiencing related complications, marking a first step in that direction.

The 2012 revised Atlanta Classification represents a global consensus that infected pancreatic necrosis serves as a key determinant of the severity in the late phase of AP.[1] Finding the best predictors of this severity variable is crucial because IPN is the primary cause of death in AP. Early triage of patients in need of transfer to a referral centre, intensive care unit (ICU) treatment, and/or particular therapies is made possible by an accurate indicator of IPN.

Healthy people have blood levels of procalcitonin that are below the clinical tests' limit of detection (0.1 μg/L). Procalcitonin synthesis is known to be triggered by bacterial toxins, such as endotoxin, and cytokines, such as TNF (Tumour Necrosis Factor)-alpha, interleukin-1-beta, and interleukin-6. However, procalcitonin can also be elevated in non-infectious causes of inflammation, such as trauma, shock, burns, and surgeries.[2] Viral or non-infectious inflammations do not cause a considerable increase in it. Procalcitonin levels in the blood can reach 100 μg/L in cases of severe infection with a corresponding systemic reaction. Procalcitonin's half-life in serum is 25 to 30 hours.[3] Acute pancreatitis and other inflammatory conditions such as bacterial sepsis, multiorgan dysfunction, and acute pancreatic necrosis are associated with elevated procalcitonin levels.[4–7] As an early indicator of the emergence of complications, we investigated the procalcitonin level during the early stages of acute pancreatitis.

MATERIALS & METHODS

This study was conducted over a period of 18 months involving 130 patients admitted to the Department of General Surgery with a history of acute upper abdominal pain with at least a threefold elevated serum amylase and/or lipase level. Patients who were diagnosed with acute pancreatitis were subjected to further investigations, including CRP, serum procalcitonin, and CECT of the upper abdomen. Those with a history of trauma, prolonged cardiogenic shock with impaired organ perfusion, lung cancer, or medullary carcinoma of the thyroid were excluded from the study. Statistical interpretation was done by analyzing the data obtained by study tools. Data analysis was done by SPSS software for Windows and the incidence was obtained. The analysis included standard diagrams and graphs, and the findings were discussed in detail to draw appropriate conclusions. Application of statistical tests was done wherever necessary.

RESULTS

The mean age of the study group was 44.3, ranging from 22 to 72 years. Mean age among males was 55.7 years, and among females was 52.6 years. Patients admitted for more than four weeks had their serum procalcitonin 37.7 ng/dl to 112.6 ng /dl. Similarly, three to four weeks of hospital admission had 1.2 ng/dl to 44.1 ng/dl. Persons with two- to three-week admissions had 0.8 ng/dl to 4.5 ng/dl and patients with less than two weeks of hospital admission had procalcitonin levels of 0.1 to 0.5 ng/dl.

Of the 130 patients, 8 persons developed massive pleural effusion, as shown in the pie diagram as a respiratory complication. 16 patients developed renal failure, 38 patients developed severe pancreatitis, of which 8 patients developed IPN (CT severity index 7 to 10), and 14 persons expired due to MODS. However, 46 patients with acute pancreatitis resolved spontaneously.

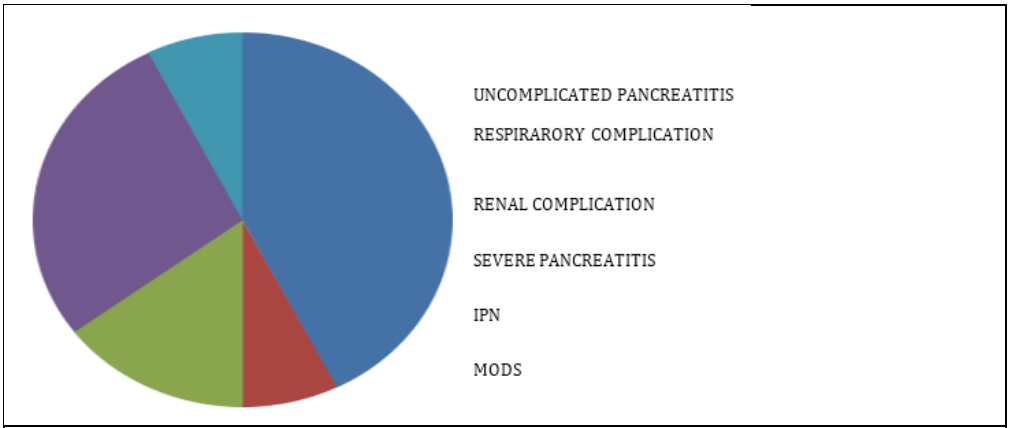

Figure 1: Incidence of Complications

Patients who had respiratory complications had a serum procalcitonin range from 16.5 to 22.7ng/dl. Among patients who had renal complications, serum procalcitonin was 15.1 to 18.3ng/dl. Similarly, patients with severe pancreatitis who developed MODS had a very high range of serum procalcitonin, 16-44.1 and 37.7-112.6 ng/dl, respectively. In uncomplicated acute pancreatitis, the PCT level was significantly low.

	Uncomplicated Pancreatitis	**Respiratory Complication**	**Renal Complication**	**Severe Pancreatitis**	**IPN**	**MODS**
Range of Serum PCT(ng/ dl)	0.1-0.5	16.5-22.7	15.1- 18.3	16-44.1	32 – 44.1	37.7-112.6

Table 1: Range of Serum PCT (ng/ dl) in Various Complications

Serum procalcitonin did not increase significantly in uncomplicated pancreatitis even after two weeks of admission, whereas in patients with MODS and severe pancreatitis, it increased significantly. Serum procalcitonin increased proportionately in different complications of acute pancreatitis.

Patient Group	**Serum PCT on Admission**	**Serum PCT after 2 Week**
Uncomplicated Pancreatitis	0.4 - 1.2	0.1 – 0.5
Respiratory Complication	4.5 – 4.9	16.5 - 22.7
Renal Complication	3.6 - 8.9	15.1 - 18.3
Severe Pancreatitis	8.8 – 19.7	16.0 -44.1
IPN	15 - 20	32 – 56.3
MODS	20.1 – 44.1	37.7 - 112.5

Table 2: Range of Serum PCT (ng/ dl) in Various Complications on Admission and after 2 Weeks

CRP level did not increase in uncomplicated pancreatitis after two weeks of admission, whereas in MODS and severe pancreatitis, it significantly increased. Also, increased values were observed in different complications of acute pancreatitis.

Patient Group	**CRP on Admission(mg/dl)**	**CRP after 2 Week(mg/dl)**
Uncomplicated Pancreatitis	2.2 – 5.5	1.2 – 3.5
Respiratory Complication	5.6 - 9.5	18.5 - 28.5
Renal Complication	5.5 – 10.5	12.5 – 15.5
Severe Pancreatitis	20.5 – 40.5	63.5 – 99.5
IPN	37.5 – 44.5	77.5 – 110.5
MODS	22.5 – 55.2	99.5 – 145.6

Table 3: Range of Serum CRP in Various Complications on Admission and after 2 Weeks

Both CRP and serum procalcitonin levels increased with an increase in the CT severity index, as shown in the table.

CRP Level (mg/dl)	Serum PCT (ng/dl)	CT Severity Index
2.1 – 2.3	0.1- 0.5	0
2.8 -3.2	0.2 – 0.5	1
4.3 – 4.6	0.8 – 1.2	2
5.8 – 7.5	1.4 – 2.2	3
10.5 – 13.4	5.5 – 10.5	4
15.6 – 18.5	13.4 – 22.5	5
22.6 – 25.6	15.5 – 27.5	6
55.2 – 77.6	22.5 – 31.2	7
80.5 – 86.4	37.7 – 40.1	8
90.3 – 99.5	33.6 – 44.1	9
110.3 – 145.6	44.6 – 112.6	10

Table 4: CRP and Serum Procalcitonin Levels and CT Severity Index

DISCUSSION

Differentiating between mild and severe cases of acute pancreatitis is the most crucial phase in the diagnosis and treatment process. Every third patient with severe acute pancreatitis may develop a microbiological infection of pancreatic necrosis despite receiving antibiotic treatment. Eighty percent of deaths from this disease are due to septic multiple organ systemic failure. Finding a trustworthy, non-invasive marker for the early detection of IPN is therefore crucial.

It has been demonstrated that PCT can distinguish between bacterial and non-bacterial (sterile) sepsis. In contrast to CRP, which distinguishes between the various types of the disease only 48 hours at the earliest, it is also a useful marker for distinguishing between necrotizing and oedematous acute pancreatitis within the first 24 hours of the beginning of symptoms. Serum PCT concentrations were compared to the control variable for pancreatic necrosis, which was the serum CRP concentration, in this investigation. There was a significant male predominance in the incidence of acute pancreatitis (4:1), and the middle-age group (35–45 years) was mainly affected.

In the study by Komalpreet Kaur et al.,[8] the mean age of participants was 38.5±11.83 years, with a range of 22-65 years, similar to our observation. There were 41 male (68.3%) and 19 female (31.6%) participants. In their investigation, procalcitonin was found to be elevated in patients with severe acute pancreatitis. This finding was receptively confirmed by two other studies conducted in Finland and Poland by Kolber et al.[9] and Back et al.[10]

While severe cases of acute pancreatitis require hospitalization in the intensive care unit, the use of antibiotics, or even surgery to address the complications, mild cases do not have any complications or organ failure and are frequently successfully treated with conservative measures. Although 15-20% of all cases appear as severe acute pancreatitis, mild and moderate cases often show little organ damage.[11] Early evaluation of each patient with acute pancreatitis can result in a precise and timely assessment of the disease's severity. The severity of acute pancreatitis can be determined using a variety of biochemical measures, CECT (Contrast Enhanced Computed Tomography) and numerous additional clinico-biochemical scores.[12,13]

Other laboratory indicators, such as the BUN (Blood Urea Nitrogen) and haemoglobin, can also help clinicians determine the severity, although in practice, no test can reliably predict the severity in individuals with acute pancreatitis.[14–16] Since it takes 72 hours to become accurate, even the most extensively researched inflammatory marker in acute pancreatitis, the acute-phase reactant CRP (C-Reactive Protein), is impractical.[17] Because necrosis typically does not appear at the outset of acute pancreatitis and develops after 48 to 72 hours, CT or MRI imaging is also not very accurate early in the course of the disease to identify severity.[18] This has made it difficult for clinicians to anticipate which patients with acute pancreatitis may progress to severe illness.

Given that procalcitonin and SAP have a positive correlation, it could be used as a predictor of SAP.[5] organ failure and pancreatic necrosis.[15] The pooled SEN, SPE, and AUC of PCT as a diagnostic marker for SAP were 0.73, 0.87, and 0.88, respectively, with a cut-off value of 0.5 ng/mL, according to a recent meta-analysis that included eight investigations.[19] In addition to CRP, PCT and interleukin-6—the gold standard for diagnosing SAP—have been documented in further research as diagnostic factors and are utilized in certain hospitals, though not regularly. Acute-phase proteins, cytokines, leukocyte-derived enzymes, antiproteases, adhesion molecules, activation peptides of pancreatic proteases, and cytokines also show encouraging outcomes but have not been used because of their poor accuracy, high cost, or difficult operation.[20] The search for novel diagnostic compounds has never ceased.

A meta-analysis by Tarján, D et al.,[21] found that the effectiveness of CRP and PCT in predicting infection in necrotizing pancreatitis can vary depending on the stage of the disease. According to earlier research by Párniczky et al., CRP, PCT, and WBC had poor predictive accuracy for infection during the first three days of admission.[22] However, CRP and PCT showed good predictive accuracy for infection after the first three days of admission, examining at least two weeks of the disease period.[23] To get more accurate results, it might be necessary to measure these biomarkers repeatedly and track them over time.

In the present study, 84 patients out of 130 developed various complications. 8 patients developed respiratory complications, 16 patients developed renal complications, 38 patients developed severe acute pancreatitis, and 8 among them developed IPN. Moderate increase of serum PCT levels found in both respiratory and renal complication groups. Unfortunately, 14 patients expired due to the development of MODS. In this group, serum PCT was also significantly increased. 46 patients were discharged without any complications with mild/no increase of serum PCT level.

The WSES 2019 guidelines state that a procalcitonin level of 3.8 ng/ml and higher, 96 hours after the disease onset, has a 93% sensitivity and a 79% specificity for indicating pancreatic necrosis.[20,24]

74 patients with acute pancreatitis were included in a Chinese study by Zhu et al. Of them, 47 patients (63.5%) had organ failure, 20 patients (27.0%) had multiple organ failure, and 27 patients (36.5%) had dysfunction of a single organ system. Among single organ failures, respiratory failure was the most prevalent organ dysfunction (23.0%; p=0.001).[25] The study by Komalpreet Kaur et al.[8] showed similar outcomes.

Although their peak is primarily seen between the second and fourth weeks after the disease's onset, the time of infection in pancreatic necrosis is variable and unpredictable. The sensitivity of clinical symptoms is good, but the specificity is inadequate. One promising serological indicator of pancreatic infection, particularly when it coexists with organ failure, is procalcitonin.[12,26]

In our study, serum PCT level was significantly increased in the IPN group. A significant increase in serum procalcitonin after 2 weeks was found in the IPN group as compared to those with severe pancreatitis only. The CTSI (CT Severity Index) was compared with serum procalcitonin level. Results showed that serum PCT level significantly increased with a CTSI score of 6 to 10.

In a related study, Volodymyr V. Kasian et al.[27] found that the procalcitonin concentration in study group patients did not surpass 3.8 ng/ml at the time of hospitalization and 72 hours later. Procalcitonin, however, is known to be a reliable indicator of both the likelihood of developing infected pancreatitis and the severity of acute pancreatitis.[28] Numerous studies show how well procalcitonin levels in the blood can be used to predict the likelihood of infected pancreatic necrosis.[29]

In the study conducted by Komalpreet Kaur et al.[8] the average CTSI score was 4.7±3.0, with a range of 1 to 10. Twenty-one individuals, particularly those with elevated procalcitonin, had CTSI scores greater than five. 18 out of 50 patients (36%) with necrotizing pancreatitis developed infected necrosis in one of the earlier studies by B. Rau et al.[30] and 11 of them passed away from septic multiple organ failure. This group's patients all had severe pancreatitis and had surgical necrosectomy with closed lavage after the procedure. Six individuals received preventive antibiotics (median start on day 3 of the disease), and four patients received antibiotics (median start on day 13 of the disease) when it was discovered that ten patients had infected necrosis during the initial surgical operation

(original infection). In contrast to the groups with oedematous pancreatitis and sterile necrosis, where PCT levels were often low or only slightly raised, individuals with infected necrosis had considerably higher median peak levels of both IL-8 and PCT. (Median PCT peaks in infected necrosis with multiple organ failure at 28.8 ng/ml, range 3.1–186.2, versus infected necrosis without multiple organ failure 3.8 ng/ml, range 1.7–5.8, $p < 0.001$) The degree of PCT elevation mirrored the systemic severity of infection in terms of related organ failure.

There was no discernible rise in PCT concentrations in individuals with sterile necrosis who had early toxic organ failure (median PCT peaks in sterile necrosis with multiple organ failure 1.0, range 0.6–1.7). Patients with infected necrosis and a complex course that led to death (n=11) had median preoperative peak PCT concentrations that were considerably lower than the maximum preoperative values (24.9 ng/ml, range 1.4–158.9 versus 3.1 ng/ml, range 0.7–26.3, $p<0.04$). On the other hand, throughout the same postoperative observation period, non-survivors had persistent median values of both measures (PCT 17.4 ng/ml, range 2.4–186, NS; IL-8 158 pg/ml, range 47–1693, NS).

CONCLUSION

Our study shows that PCT closely correlates with both infected necrosis and the severity of associated systemic complications. PCT could be a potential independent new indicator for selecting patients with acute pancreatitis at risk of developing infectious necrosis and provide valuable information on the severity of septic complications in critically ill patients.

REFERENCES

[1] Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102-11.
[2] Becker KL, Snider R, Nylen ES. Procalcitonin assay in systemic inflammation, infection, and sepsis: clinical utility and limitations. Crit Care Med 2008;36(3):941-52.
[3] Goldie AS, Ross JA, Carter DC, et al. Serum concentrations of inflammatory mediators related to organ failure in patients with acute pancreatitis. Br J Surg 1996;83(3):349-53.
[4] AI-Nawasl B, Krammer I, Shah PM. Procalcitonin in diagnosis of severe infections. Eur J Med 1996;1(7):331-3.
[5] Mandi Y, Farkas G, Takacs T, et al. Diagnostic relevance of procalcitonin, IL-6, and sICAM-1 in the prediction of infected necrosis in acute pancreatitis. Int J Pancreatol 2001;28 (1):41-9.
[6] Dogru O, Ayten R, Ilhan YS, et al. Procalcitonin is a predictive marker for severe acute pancreatitis. Ulus Travma Acil Cerrahi Derg 2006;12 (2):115-20.
[7] Mofidi R, Suttie SA, Parks RW, et al. The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: systematic review. Surgery 2009;146 (1):72-81.
[8] Kaur K, Singh K. Evaluation of pro calcitonin as an early prognostic marker in acute pancreatitis. J Evid Based Med Healthc 2020;7(5):203-7.
[9] Kolber W, Kusnierz-Cabala B, Dumnicka P, et al. Serum urokinase-type plasminogen activator receptor does not outperform C-reactive protein and procalcitonin as an early marker of severity of acute pancreatitis. J Clin Med 2018;7(10):305.
[10] Kylänpää-Bäck ML, Takala A, Kemppainen EA, et al. Procalcitonin, soluble interleukin-2 receptor, and soluble E-selectin in predicting the severity of acute pancreatitis. Crit Care Med 2001;29(1):63-9.
[11] Ranson JH, Pasterneck BS. Statistical method for quantifying the severity of acute pancreatitis. J Surg Res 1997;22(2):79-91.
[12] Knaus WA, Draper EA, Wagner DP. APACHE II: a severity of disease classification system. Crit Care Med 1985;13(10):818-29.
[13] Wu BU, Johannes RS, Sun X, et al. The early prediction of mortality in acute pancreatitis: a large population based study. Gut 2008;57(12):1698-703.

[14] Mounzer R, Langmead CJ, Wu BU, et al. Comparison of existing clinical scoring systems to predict persistent organ failure in patients with acute pancreatitis. Gastroenterology 2012;142(7):1476-82.
[15] Lankisch PG, Mahlke R, Blum T, et al. Hemoconcentration: an early marker of severe and/or necrotizing pancreatitis? A critical appraisal. Am J Gastenterol 2001;96(7):2081-5.
[16] Frossard JL, Hadengue A, Pastor CM. New serum markers for the detection of severe acute pancreatitis in humans. Am J Respir Crit Care Med 2001;164(1):162-70.
[17] Papachristou GI, Whitcomb DC. Inflammatory markers of disease severity in acute pancreatitis Clin Lab Med 2005;25(1):17-37.
[18] Freeman MF, Werner J, van Santvoort HC, et al. Intervention for necrotising pancreatitis: summary of multidisciplinary consensus conference. Pancreas 2012;41(8):1176-94.
[19] Mofidi R, Suttie SA, Patil PV, et al. The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: systematic review. Surgery 2009;146(1):72-81.
[20] Staubli SM, Oertli D, Nebiker CA. Laboratory markers predicting severity of acute pancreatitis. Crit Rev Clin Lab Sci 2015;52(6):273-83.
[21] Tarján D, Szalai E, Lipp M, et al. Persistently high procalcitonin and C-Reactive protein are good predictors of infection in acute necrotizing pancreatitis: a systematic review and meta-analysis. Int J Mol Sci 2024;25:1273.
[22] Li F, He H. Assessing the accuracy of diagnostic tests. Shanghai Arch Psychiatry 2018;30:207-12.
[23] Rutter CM, Gatsonis CA. A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. Stat Med 2001;20:2865-84.
[24] Yang CJ, Chen J, Phillips ARJ, et al. Predictors of severe and critical acute pancreatitis: a systematic review. Dig Liver Dis 2014;46(5):446-51.
[25] Zhu AJ, Shi JS, Sun XJ. Organ failure associated with severe acute pancreatitis. World J Gastroenterol 2003;9(11):2570-3.
[26] Rau BM, Kemppainen EA, Gumbs AA, et al. Early assessment of pancreatic infections and overall prognosis in severe acute pancreatitis by procalcitonin (PCT). Ann Surg 2007;245(5):745-54.
[27] Kasian VV, Sheiko VD, Mamontova TV, et al. Procalcitonin in early prediction of acute severe pancreatitis. Wiad Lek 2020;73(7):1370-2.
[28] Assicot M, Gendrel D, Carsin H. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 1993;(341):515-8.
[29] Chen HZ, Ji L, Li L, et al. Early prediction of infected pancreatic necrosis secondary to necrotizing pancreatitis. Med (United States) 2017;96(30):e7487.
[30] Rau B, Steinbach G, Gansauge F, et al. The potential role of procalcitonin and interleukin 8 in the prediction of infected necrosis in acute pancreatitis. Gut 1997;41:832-40.