How to Cite:
Surana, P., Kumar, V. S., Patro, B., & Shanmugasundaram, P. N. (2022). Procalcitonin as a predictor of severity in acute pancreatitis: An observational study. *International Journal of Health Sciences*, *6*(S2), 10917–10923. https://doi.org/10.53730/ijhs.v6nS2.7933

Procalcitonin as a predictor of severity in acute pancreatitis: An observational study

Dr Pankaj Surana
MS, Associate Professor, Department of General Surgery, ESIC Medical College And PGIMSR, KK Nagar Chennai, Tamilnadu

Dr V Sarath Kumar
MS, Senior Resident, Department of General Surgery, ESIC Medical College and PGIMSR, KK Nagar Chennai, Tamilnadu

Dr Byomokesh Patro
MS, Assistant Professor, Department of General Surgery, ESIC Medical College and PGIMSR, Chennai, Tamilnadu
Corresponding author email: byomkesh.patro@gmail.com

Dr P N Shanmugasundaram
MS, Professor, Department of General Surgery, ESIC Medical College and PGIMSR, KK Nagar Chennai, Tamilnadu

***Abstract*---**Background: Outcomes and severity of acute pancreatitis is a challenging condition to diagnose. However, multiple clinico-biochemical scores, imaging, radiological imaging, and biochemical markers are used. Aims: To evaluate procalcitonin as a predictor of severity in acute pancreatitis and to correlate the levels of procalcitonin to the CT Severity Index score. Materials and Methods: In 65 study subjects, prolactin levels, CRP, blood glucose, liver function tests, BUN, creatinine, urea, CBC, and radiological investigations including whole abdomen USG, X-ray abdomen-supine and erect, and chest X-ray PA view. Following 48-72 hours of admission, a CT abdomen was done on subjects with diagnostic dilemmas. In subjects where CECT was done, necrosis scores and Balthazar grading were used for grading the CT severity index. Results: For the cut-off PCT value of 1.77 ng/ml the sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 74.8, 76.88, 74.8, 76.94, 74, and 15.154 respective. In the PCT cut-off value of 3.29 ng/ml, the respective values of sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 66.65, 84.58, 79.8, 73.31, 74, and 14.426. BCTSI score of ≥4, the respective values of sensitivity, specificity, PPV, NPV, accuracy and likelihood ratio were 62.3, 65.36, 62.3, 65.36, 65, and 3.936. Conclusion: In subjects with acute

Manuscript submitted: 27 March 2022, Manuscript revised: 09 April 2022, Accepted for publication: 18 May 2022

pancreatitis, levels of serum Prolactin help in the accurate identification of subjects that ware likely to progress to severe acute pancreatitis.

***Keywords*---**pancreatitis, serum prolactin, CRP, CBC.

Introduction

Acute pancreatitis signifies an inflammatory condition presenting with a wide range of clinical and morphological manifestations. Acute pancreatitis is also associated with high mortality rates from 25% to nearly 50% and is a major cause of pancreatic necrosis and MOF (multiple organ failure). Prediction of outcomes and severity of acute pancreatitis is a challenging condition for most clinicians. However, early diagnosis and regular monitoring of subjects with acute pancreatitis are vital for preventing complications and providing needed treatment. To assess the outcomes and disease severity, multiple clinico-biochemical scores, imaging, radiological imaging, and biochemical markers are used.[1]

The prognostic methods should be inexpensive, accurate, and simple. These criteria are fulfilled by PCT (Procalcitonin) which is an inflammatory cell product, all differentiated cell types, and all parenchymal tissues including muscles, adipose tissues, kidneys, and the liver in response to the inflammatory mediators. Procalcitonin is a marker of systemic inflammation which is seen in early conditions of inflammation, multi-organ failure, and sepsis. Previous literature data has shown that PCT is a reliable and early biomarker and predictor of acute pancreatitis, related death, and infected pancreatic necrosis.[2] PCT is a calcitonin hormone precursor responsible for calcium hemostasis and is produced by the intestine, neuroendocrine cells of the lungs, and parafollicular C cells of the thyroid. In healthy subjects, PCT is not assessed in the blood (0.01 mcg/L). PCT level increase following bacterial and other proinflammatory stimulus, and is hence considered an acute phase reactant. PCT levels can increase significantly up to 100mcg/L in severe infections and has a half-life of nearly 30 hours. Despite low PCT blood levels, it can be a reliable sepsis marker and its levels have been linked to sepsis severity. In comparison with TNF alpha, CRP, IL-6, and IL-2, PCT can differentiate SIRS (systemic inflammatory response syndrome) from sepsis with high specificity and sensitivity.[3]

For acute pancreatitis, various scoring systems have been developed to assess severity. However, for predicting the severity of acute pancreatitis, these systems are not convenient as they include different parameters. These scoring systems include CTSI (computed tomography severity index), APACHE II (Acute Physiology and Chronic Health Evaluation), and Ranson criteria. However, these systems have few limitations including the requirement of rarely needed data and associated complexity making the early stage risk stratification difficult. Scoring systems such as Atlanta scores and Balthazar Grade have helped to overcome these limitations to some extent.[4] Hence, the present clinical study was conducted to evaluate procalcitonin as a predictor of severity in acute pancreatitis and to correlate the levels of procalcitonin to the CT Severity Index score.

Materials and Methods

The present non-randomized observational clinical study was conducted to evaluate procalcitonin as a predictor of severity in acute pancreatitis and to correlate the levels of procalcitonin to the CT severity index score. The present study was conducted for 1 year period at the Department of General Surgery, ESIC Medical College &PGIMSR Chennai after obtaining clearance from the concerned Ethicaln Committee. The study population comprised of the subjects visiting the Department of Surgery of the Institute. The study included a total of 65 subjects from both genders. The inclusion criteria for the study were subjects of age 18 years or more with acute pancreatitis and the subjects who were willing to participate in the study. The exclusion criteria for the study were subjects with associated conditions like bronchitis, pneumonia, or acute exacerbation of COPD, and subjects having other associated abdominal conditions like acute cholecystitis and peritonitis due to other reasons.

For estimated sensitivity of 86% (Bezmarevic M, Kastic Z, et al. Procalcitonin and BISAP score versus C- reactive protein and APACHE-II score in early assessment of severity and outcome of acute pancreatitis, Vrjnosanit Pregl, 2012, May) with 95 % confidence and 10% relative precision of the estimate, the sample size was calculated as 65. After the final inclusion of the study subjects with pancreatitis, the subjects were admitted to the Department of General Surgery where the detailed history of the subjects was taken followed by a clinical examination and required laboratory investigations. For laboratory investigations, intravenous blood was collected from all the subjects in sterile and aseptic conditions and the investigations done were prolactin levels, CRP (C-reactive protein), blood glucose, liver function tests, BUN (blood urea nitrogen), creatinine, urea, and CBC (complete blood counts). This was followed by radiological investigations including whole abdomen USG, X-ray abdomen-supine and erect, and chest X-ray PA view. Following 48-72 hours of admission, a CT scan of the abdomen was done on subjects with diagnostic dilemmas. In subjects where CECT was done, necrosis scores and Balthazar grading[5] were used for grading the CT severity index. The subjects were graded as mild, moderate, or severe based on the Atlanta Criteria[6] of 2012. The collected data were subjected to the statistical evaluation utilizing inferential and descriptive analysis evaluation using SPSS software version 21 (Chicago, IL, USA) and one-way ANOVA and t-test for results formulation. The data were expressed in percentage and number, and mean and standard deviation. The level of significance was kept at $p<0.05$.

Results

The present non-randomized observational clinical study was conducted to evaluate procalcitonin as a predictor of severity in acute pancreatitis and to correlate the levels of procalcitonin to the CT Severity Index score. The study included a total of 65 subjects from both genders. The demographic characteristics of the study subjects are listed in Table 1. Based on Atlanta's criteria, mild pancreatitis was seen in 52.30% (n=34) subjects and severe pancreatitis was seen in 47.69% (n=31) study subjects. The mean age of the subjects was 59.3±1.42 years. In mild pancreatitis and severe pancreatitis group, the mean age and gender have no statistical difference with p=0.226 and 0.852

respectively. 2.94% (n=1) of subjects died in the mild pancreatitis group, and the mortality in the severe pancreatitis group was 22.58% (n=7) which was significantly higher in the severe pancreatitis group with p=0.03. The most common etiology in both groups was alcohol intake with 41.17% (n=14) in mild and 54.83% (n=17) in severe pancreatitis group followed by Miscellaneous and Idiopathic and biliary in 29.41% (n=10) subjects in the mild group, and 29.03% (n=9) and 16.12% (n=5) in severe pancreatitis group. PCT values were significantly higher in the severe pancreatitis group (1.64±3.64 ng/ml) compared to mild pancreatitis (0.41±3.68) with p=0.001. Similar results were seen for necrosis with 0 and 70.96% (n=22) respectively with p<0.001. Urea and CRP levels were significantly higher in severe pancreatitis compared to mild pancreatitis with p=0.01. The mean Balthazar CT severity score index (BCTSI) was 2 in mild pancreatitis and 3 in severe pancreatitis which was significantly higher with p=0.02 (Table 1).

For Procalcitonin, various cut-off values were taken and its reliability was assessed as a predictor of acute pancreatitis severity. The cut-off values taken were 0.50, 1.00, 1.77, and 3.29 ng/ml in the present study. For the PCT value of 0.50 ng/ml the sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 87.3, 53.06, 51.24, 66.65, 52, and 11.33 respectively. For the cut-off PCT value of 1.00 ng/ml, the respective values of sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 83.31, 65.36, 68.95, 80.93, 72, and 12.863. For the cut-off PCT value of 1.77 ng/ml the sensitivity, specificity, PPV, NPV, accuracy and likelihood ratio were 74.8, 76.88, 74.8, 76.94, 74, and 15.154 respective. In the PCT cut-off value of 3.29 ng/ml, the respective values of sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 66.65, 84.58, 79.8, 73.31, 74, and 14.426 as shown in Table 2. High sensitivity, specificity, and accuracy were seen for PCT values of 1.00, 1.77, and 3.29 ng/ml. Statistical significance was seen for PCT value in predicting acute pancreatitis severity.

The accuracy of the study parameters was assessed in severe acute pancreatitis. For PCT of ≥ 3.29 ng/ml, the sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 66.65, 84.64, 79.8, 73.31, 78, and 14.422 respectively, whereas, for Balthazar CT severity score index (BCTSI) score of ≥4, the respective values of sensitivity, specificity, PPV, NPV, accuracy and likelihood ratio were 62.3, 65.36, 62.3, 65.36, 65, and 3.936 as depicted in Table 3.

Discussion

The present non-randomized observational clinical study was conducted to evaluate procalcitonin as a predictor of severity in acute pancreatitis and to correlate the levels of procalcitonin to the CT Severity Index score. The study included a total of 65 subjects from both genders. Based on Atlanta's criteria, mild pancreatitis was seen in 52.30% (n=34) subjects and severe pancreatitis was seen in 47.69% (n=31) study subjects. The mean age of the subjects was 59.3±1.42 years. In mild pancreatitis and severe pancreatitis group, the mean age and gender have no statistical difference with p=0.226 and 0.852 respectively. 2.94% (n=1) of subjects died in the mild pancreatitis group, and the mortality in the severe pancreatitis group was 22.58% (n=7) which was significantly higher in

the severe pancreatitis group with p=0.03. The most common etiology in both groups was alcohol intake with 41.17% (n=14) in mild and 54.83% (n=17) in severe pancreatitis group followed by Miscellaneous and Idiopathic and biliary in 29.41% (n=10) subjects in the mild group, and 29.03% (n=9) and 16.12% (n=5) in severe pancreatitis group. PCT values were significantly higher in the severe pancreatitis group (1.64±3.64 ng/ml) compared to mild pancreatitis (0.41±3.68) with p=0.001. Similar results were seen for necrosis with 0 and 70.96% (n=22) respectively with p<0.001. Urea and CRP levels were significantly higher in severe pancreatitis compared to mild pancreatitis with p=0.01. The mean Balthazar CT severity score index (BCTSI) was 2 in mild pancreatitis and 3 in severe pancreatitis which was significantly higher with p=0.02. These demographics were comparable to the studies of Mofidi R et al[7] in 2009 and Rau BM et al[8] in 2007 where authors assessed subjects with demographics comparable to the present study.

Concerning Procalcitonin, various cut-off values were taken and its reliability was assessed as a predictor of acute pancreatitis severity. The cut-off values taken were 0.50, 1.00, 1.77, and 3.29 ng/ml in the present study. For the PCT value of 0.50 ng/ml the sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 87.3, 53.06, 51.24, 66.65, 52, and 11.33 respectively. For the cut-off PCT value of 1.00 ng/ml, the respective values of sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 83.31, 65.36, 68.95, 80.93, 72, and 12.863. For the cut-off PCT value of 1.77 ng/ml the sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 74.8, 76.88, 74.8, 76.94, 74, and 15.154 respective. In the PCT cut-off value of 3.29 ng/ml, the respective values of sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 66.65, 84.58, 79.8, 73.31, 74, and 14.426. High sensitivity, specificity, and accuracy were seen for PCT values of 1.00, 1.77, and 3.29 ng/ml. Statistical significance was seen for PCT value in predicting acute pancreatitis severity. These results were consistent with the studies of Woo SM et al[9] in 2011 and Kumar S et al[10] in 2017 where authors reported comparable sensitivity, specificity, and accuracy of PCT cut-off values in their studies.

The accuracy of the study parameters was assessed in severe acute pancreatitis. For PCT of ≥ 3.29 ng/ml, the sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratio were 66.65, 84.64, 79.8, 73.31, 78, and 14.422 respectively, whereas, for Balthazar CT severity score index (BCTSI) score of ≥4, the respective values of sensitivity, specificity, PPV, NPV, accuracy and likelihood ratio were 62.3, 65.36, 62.3, 65.36, 65, and 3.936. These findings were in agreement with the findings of Li Y et al[11] in 2017 and Zhou H et al[12] in 2019 where reported parameters of the present study as compared to the studies of these authors.

Conclusion

Within its limitations, the present study concludes that in subjects with acute pancreatitis, levels of serum Prolactin help in the accurate identification of subjects that will likely to progress to severe acute pancreatitis, and is a reliable prognostic indicator of disease severity. Also, the Balthazar score is a better prognostic indicator than other blood parameters for assessing the disease severity of acute pancreatitis. The present study had a few limitations including

small sample size, shorter monitoring period, and geographical area biases. Hence, more longitudinal studies with larger sample size and longer monitoring period will help reach a definitive conclusion.

Type of study: Original Research Paper
Conflicts of interest: Nil

References

1. Shah AP, Mourad MM, Bramhall SR. Acute pancreatitis: Current perspectives on diagnosis and management. J Inflamm Res. 2018;11:77–85.
2. Cho JH, KimTN, Chung HH & Kim KH. Comparison of scoring systems in predicting the severity of acute pancreatitis. World J Gastroenterol 2015;21:2387-94.
3. Gurda-Duda A, Kusnierz-Cabala B, Nowak W, Naskalski JW, Kulig J. Assessment of the prognostic value of certain acute-phase proteins and procalcitonin in the prognosis of acute pancreatitis. Pancreas. 2008;37:449–53.
4. O'Connell RM, Boland MR, O'Driscoll J, Salih A, Arumugasamy M, Walsh TN, et al. Red cell distribution width and neutrophil to lymphocyte ratio as predictors of outcomes in acute pancreatitis: A retrospective cohort study. Int J Surg. 2018;55:124–7.
5. Balthazar EJ et al. Acute pancreatitis: prognostic value of CT Radiology. 1985;156:767-72
6. Peter A Banks et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus Gut. 2013;62:102-11.
7. Mofidi R, Suttie SA, Patil PV, Ogston S and Parks RW. The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: a systematic review. Surgery 2009;146:72-81
8. RauBM, Kemppainen EA, Gumbus AA, Buchler MW, Wegscheider K, Bassi C, PuolakkainenPA and Beger HG. Early Assessment of Pancreatic Infections and Overall Prognosis in Severe Acute Pancreatitis by Procalcitonin (PCT). Ann Surg. 2007;245:745–54.
9. Woo SM, Noh MH, Kim BG, Hsing CT, Han JS, Ryu SH, Seo JM, Yoon HA, Jang JS, Choi SR, and Cho JH. Comparison of serum procalcitonin with Ranson, APACHE-II, Glasgow, and Balthazar CT severity index scores in predicting the severity of acute pancreatitis. Korean J Gastroenterol 2011;58:31-7.
10. Kumar S, Jalan A, Patowary BN, et al. To access the role of serum procalcitonin in predicting the severity of acute pancreatitis. Kathmandu Univ Med J. 2017;15:19–24.
11. Li Y, Zhao Y, Feng L, Guo R. Comparison of the prognostic values of inflammation markers in patients with acute pancreatitis: A retrospective cohort study. BMJ Open. 2017;7:013206.
12. Zhou H, Mei X, He X, Lan T, Guo S. Severity stratification and prognostic prediction of patients with acute pancreatitis at early phase: A retrospective study. Medicine (Baltimore) 2019;98:e15275.

Tables

Characteristics	Mild pancreatitis (n=34)	Severe Pancreatitis (n=31)	Total (n=65)	p-value
Mean age (years)	54.3±1.46	64.3±1.44	59.3±1.42	0.226
Gender % (n)				
Males	67.64 (23)	67.74 (21)	67.69 (44)	0.852
Females	32.35 (11)	32.25 (10)	32.30 (21)	
Mortality % (n)	2.94 (1)	22.58 (7)	12.30 (8)	0.03
Hospital stay duration (days)	11.3±2.4	18.3±2.6	15.3±2.3	0.154
Disease etiology				
Biliary	29.41 (10)	16.12 (5)	23.07 (15)	-
Alcohol	41.17 (14)	54.83 (17)	47.69 (31)	-
Miscellaneous and Idiopathic	29.41 (10)	29.03 (9)	29.23 (19)	-
Laboratory parameters (mean)				
Urea	16.3±2.4	28.3±2.6	19.3±2.2	0.01
Glucose	128.4±6.28	157.2±6.22	138.3±6.24	0.114
CRP	3.67±4.12	11.71±4.14	7.7±4.13	0.01
PCT (ng/ml)	0.41±3.68	4.26±3.66	1.64±3.64	0.001
Necrosis (n=23)	0	70.96 (22)	33.84 (22)	<0.001
BCTSI scoring	2	3	2	0.02

Table 1: Demographic characteristics of the study subjects

PCT Value (cut-off) ng/ml	Sensitivity (%)	Specificity (%)	PPV (positive predictive value) (%)	NPV (negative predictive value) (%)	Accuracy (%)	Likelihood ratio
0.50	87.3	53.06	51.24	66.65	52	11.833
1.00	83.31	65.36	68.95	80.93	72	12.863
1.77	74.8	76.88	74.8	76.94	74	15.154
3.29	66.65	84.58	79.8	73.31	74	14.426

Table 2: Accuracy of PCT in assessing acute pancreatitis in the study subjects

Parameter	Sensitivity (%)	Specificity (%)	PPV (positive predictive value) (%)	NPV (negative predictive value) (%)	Accuracy (%)	Likelihood ratio
PCT ≥3.29 ng/ml	66.65	84.64	79.8	73.31	78	14.422
BCTSI ≥4	62.3	65.36	62.3	65.36	65	3.936

Table 3: Accuracy of the study parameters