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C-reactive protein and modified computed tomography severity index in assessing severity of acute pancreatitis

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ABSTRACT

Background: The mortality and morbidity associated with acute pancreatitis (AP) demands timely management and prediction of disease progression and clinical outcome. Multifactorial scoring systems shall facilitate risk stratification and prognostic assessment in AP. **Aims and Objectives:** The aim of the study was (i) to assess C-reactive protein (CRP) levels and modified computed tomography severity index (mCTSI) in AP patients and their association with the clinical outcome and (ii) to determine the correlation between CRP levels and mCTSI scores in AP. **Materials and Methods:** This cross-sectional, hospital-based study comprised 90 patients diagnosed with AP. Data collection included sociodemographic information, clinical presentation, and CRP estimation. The mCTSI score was estimated by axial slices contrast-enhanced computed tomography of abdomen and was used to assess the severity of AP. Categorical data were analyzed by Chi-square test and Pearson's coefficient was estimated to determine the correlation between CRP levels and mCTSI score. $P<0.05$ was adopted as level of significance. **Results:** The study comprised 81 males (90%) and 9 females (10%). The mean age of the patients was 36.94 ± 9.19 years, with majority in age group of 31–40 years (40%). Alcohol consumption (>50 g/day) was the commonest risk factor in 82.22% (n = 74) patients, followed by hypertriglyceridemia in 13.33% (n = 12) patients. Pain in abdomen was the most common presentation in 96.67% (n = 87) patients, followed by vomiting 57.78% (n = 52) patients. Majority of patients [82.22% (n = 74)] had CRP levels of 10–21 mg/dL. Mild, moderate, and severe mCTSI scores were obtained in 17.78%, 66.67%, and 15.55% patients, respectively. There is a significant positive correlation between CRP values and mCTSI scores with $r = 0.3008$ ($P = 0.003$). **Conclusion:** CRP level had significant positive correlation with mCTSI scores in AP. Higher values of CRP and severe mCTSI scores had worse clinical outcome in AP.

Key words: Acute pancreatitis; Modified computed tomography severity index; C-reactive protein

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INTRODUCTION

The pathophysiology of acute pancreatitis (AP) revolves around unregulated proteolytic enzymatic activation causing autodigestion and inflammation of pancreas.[1] The severity is variable with majority experiencing mild, self-resolving symptoms, while few carry the risk of complications and substantial mortality. Due to the unpredictable clinical course, multifactorial scoring systems have been developed combining laboratory investigations,

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clinical presentation, and radiological findings to predict severity index and monitor disease progression.[2] An ideal prognostic assessment that facilitates risk stratification of pancreatitis patients should be easily available with least interobserver variability.

C-reactive protein (CRP), an acute reactant protein, is synthesized in liver in response to inflammation-induced cytokines in AP.[3] Khanna et al., concluded CRP to have 100% sensitivity and 81.4% specificity for prediction of AP-related complications and mortality.[2] Contrast enhanced computed tomography (CECT) is the gold standard imaging modality in AP evaluation.[4] In addition to the diagnosis of AP, CECT also highlights the evidence and extent of pancreatic necrosis. The modified computed tomography severity index (mCTSI) by Mortele et al., utilizes pancreatic inflammation, necrosis, and extra-pancreatic complications as prognostic indicators to yield the final score.[5] It has 40% sensitivity, 67% negative predictive value, and 100% positive predictive value for the detection of severe pancraetitis.[6] The revised Atlantic classification on AP 2012 has been adopted for standardized reporting and stratification of patients based on clinical and radiological criteria.[7] The grades of severity (mild, moderate, and severe) depend on the combination of the local and systemic complications.

The surge in incidence of AP can be attributed to constellation of factors which include uptrend in gall stones, obesity, and hypertriglyceridemia incidence as well as lifestyle trends like increased alcohol and tobacco consumption.8 Thus, due to the multifactorial nature of etiopathogenesis in AP, it is imperative to predict the severity of AP at the time of presentation for early escalation of care and aggressive management and to reduce the disease associated morbidity and mortality.

Aims and objectives

The primary objective of the study was to assess CRP levels and mCTSI scores in AP patients. The secondary objectives were i) to determine association of CRP levels and mCTSI scores with the clinical outcome in patients with AP, ii) to determine the correlation between CRP levels and mCTSI in AP.

MATERIALS AND METHODS

This was a cross-sectional, hospital-based study conducted in the Department of General Medicine for a period of 1 year from July 1, 2020, to June 30, 2021. The study protocol was approved by Institutional Ethical Committee reference ID: SMEJ/JMCH/MEU/841/Pt-1/2011/5496 dated June 30, 2020. The study was conducted according to the guidelines of Declarations of Helsinki and Good Clinical Practice requirements. Participation was voluntary and no rewards/incentive was awarded. Informed written consent was obtained from each participant with guarantee of anonymity of collected data.

The patients with diagnosis of AP as per revised Atlantic classification 2012 served as the cohort for the study.[7] Patients with more than 18 years of age and willing to participate were included in the study. The exclusion criteria included (a) diagnosis of chronic pancreatitis, (b) trauma as the cause of AP, (c) clinically unstable patient, (d) severe co-morbid conditions like hepatic/renal failure, malignancy, (e) severe cognitive impairment, (f) pregnancy and lactation, and (g) refusal for participation.

Sample size estimation and sampling method

The sample size was estimated using 6% as the prevalence of AP as per previous studies.[9] Taking into consideration 95% as the confidence interval (CI) and 5% as the relative error, the sample size was calculated to be 90 using the formula.

$$\text{Sample size} = 4PQ/E^2$$

where P=0.06, prevalence of AP, Q=100–P and E=0.05, allowable error at 95% CI.

The recruitment of the participants in the study was based on non-probability consecutive sampling.

Data collection

The selected participants more than 18 years of age were subjected to face-to-face interviews and clinical examination. The socio-demographic data included age, gender, marital status, educational qualification, medical history, drug history, family history, and history of substance abuse. The clinical presentation of each patient and physical examination findings was documented.

Estimation of CRP levels

The blood sample was collected within 24 h of admission. With aseptic precautions, 2 mL of venous blood was collected in the clot activator vial. The sample was processed in the Institutional Central Laboratory on the same day. The quantitative estimation of CRP was done using Nephelometric method in Mispa i2. CRP value more than 10 mg/dL was considered significant.[10]

Estimation of mCTSI

The patient was subjected to CECT scan within 24 h of hospitalization and clinical stabilization. The CECT scan was performed utilizing instrument Philips 16 slice computed tomography (CT) machine and axial slices of abdomen of 3 mm thickness were obtained. The mCTSI was estimated

based on the parameters tied in Table 1.[5] The sum of the parameters yielded the final scores ranging from "0" to "10." The scores "0–2", "4–6", and "8–10" were considered as mild, moderate, and severe grade of pancreatitis, respectively.

Statistical analysis

The collected data were quality checked for its completeness and accuracy. It was organized into Microsoft Excel spreadsheet and Statistical Package for the Social Sciences version-26 was utilized for statistical analyses. The continuous variables were expressed as mean and standard deviation. Categorial data were computed into frequency (No) and percentages (%). Chi-square (χ^2) test was used to determine the statistical difference between the categorical variables. Pearson's correlation was utilized to determine the correlation between CRP values and mCTSI scores. For all statistical analyses, $P<0.05$ was adopted as level of significance.

RESULTS

A total of 122 patients with clinical presentation of AP were screened for inclusion into the study. However, 32 patients were excluded from the study due to the reasons tied in Figure 1. Hence, the data analysis was limited to 90 patients.

Among 90 patients with diagnosis of AP, majority were males [n=81 (90%)]. The socio-demographic characteristics and clinical course of the participants are displayed in Table 2. The mean age of the participants is 36.94±9.19 years, with majority (40%) in the age group of 31–40 years. Alcohol consumption was present in 91.11% (n=82) of the patients of which 82.22% (n=74) consumed more than 50 g/day. Pain in abdomen was the most common presentation in 96.67% (n=87) patients, followed by vomiting in 57.78% (n=52) patients Majority of the patients [n=61 (67.78%)] were hospitalized for 5–7 days. Mortality was seen in 6.67% (n=6) patients admitted for AP.

Majority of AP patients [82.22% (n=74)] had CRP levels of 10–21 mg/dL as shown in Figure 2. All four patients with CRP value <10 mg/dL were discharged (Table 3). Mortality was observed among one patient (out of 74) and seven patients (out of 12) with CRP values 10–21 mg/dL and >21 mg/dL, respectively. The association between CRP values and clinical outcome was statistically significant (P=0.00002) as citied in Table 3.

Mild, moderate, and severe mCTSI scores were obtained in 17.78%, 66.67%, and 15.55% patients, respectively (Figure 3). All patients with mild and moderate mCTSI scores were discharged (Table 3). However, mortality was observed in six patients (out of 14) with severe mCTSI score.

Table 1: Modified CT severity index in acute pancreatitis[5]

Prognostic indicators	Categories	Points
Pancreatic inflammation	Normal pancreas	0
	Intrinsic pancreatic abnormalities with or without inflammatory changes in peripancreatic fat	2
	Pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis	4
Pancreatic necrosis	None	0
	≤30%	2
	>30%	4
Extra-pancreatic complications	One or more of pleural effusion, ascites, vascular complications, parenchymal complications, or gastrointestinal tract involvement	2

CT: Computed tomography

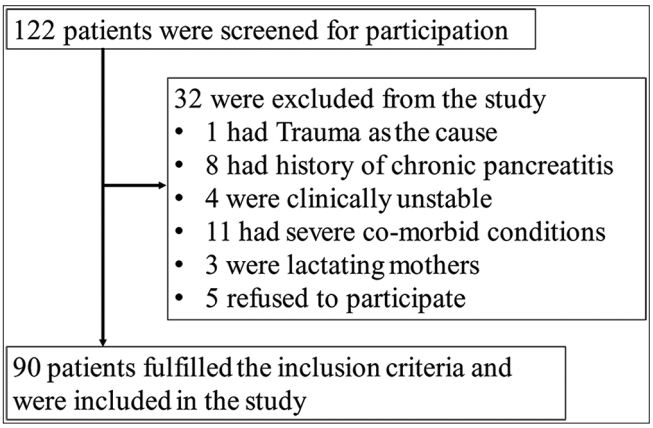

Figure 1: Flowchart of present study showing recruitment of participants

The association between mCTSI scores and the clinical outcome was statistically significant (P=0.000001) as per Table 3. There is a significant positive correlation between CRP values and mCTSI scores with r=0.3008 (P=0.003) (Figure 4).

DISCUSSION

AP is one of the most gastrointestinal emergencies encountered with high mortality rates if not intervened promptly and aggressively. The mortality associated with AP in early phase can be attributed to the development and progression of organ dysfunction with is consistent with extent of inflammation and cellular injury.[11] Arrest or reversal of early organ dysfunction has a key role in attenuating morbidity and mortality in AP patients. Development of scoring systems has aided the patient stratification and management.

Table 2: Socio-demographic characteristics and clinical information of patients with acute pancreatitis

Variables	Categories	No (%)
Age (in years)	18–30	25 (27.78)
	31–40	36 (40)
	41–50	14 (15.56)
	51–60	6 (6.66)
	>60	9 (10)
Gender	Male	81 (90)
	Female	9 (10)
Substance abuse	Alcohol	82 (91.11)
	Smoking	21 (23.33)
	Drug abuse	0 (0)
Risk factors	Alcohol (>50 g/day)	74 (82.22)
	Gall stones	4 (4.44)
	Hypertriglyceridemia	12 (13.33)
Presenting symptoms	Pain in abdomen	87 (96.67)
	Vomiting	52 (57.78)
	Constipation	37 (41.11)
	Difficulty in breathing	17 (18.89)
	Jaundice	9 (10)
Duration of hospitalization	<5 days	4 (4.44)
	5–7 days	61 (67.78)
	8–10 days	20 (22.22)
	>10 days	5 (5.56)
Outcome	Discharged	84 (93.33)
	Death	6 (6.67)

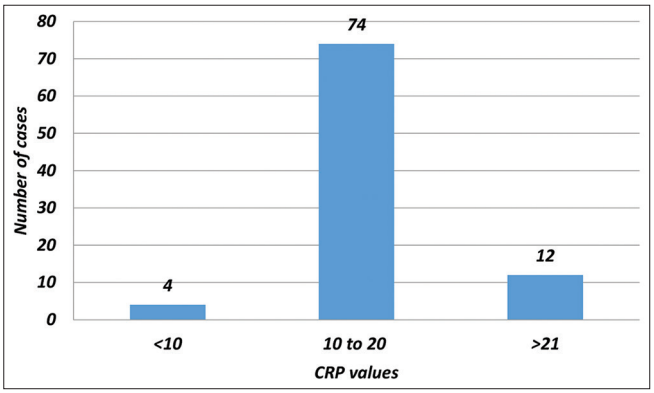

Figure 2: C-reactive protein values in patients with acute pancreatitis

The present study revealed preponderance of males [n=81 (90%)] patients, similar to observations by Li et al.[12] Higher prevalence was observed among age group 31–40 years. Similar observations have been seen in studies in AP patients by Vengadakrishnan and Koushik.[13] In the present study, pain in abdomen was the most common presentation, similar to many observational studies.[14] Alcohol was the commonest risk factor among majority of the hospitalized patients. A prospective cohort study on metabolic and lifestyle risk factors for AP in 0.5 million people highlighted the adjusted hazard ratio of 1.52 and 1.45 among alcoholics and smokers, respectively.[15] Experimental models have revealed direct ethanol-induced zymogen activation of pancreatic acinar cells which effectuates as proteolysis, inflammation, and tissue necrosis.[16]

In the present study, mortality was observed among one patient (out of 74) and seven patients (out of 12) with CRP values 10–21 mg/dL and >21 mg/dL, respectively, and CRP values had significant association with clinical outcome. Thus, CRP is a valuable predictor of severity in AP, especially to detect pancreatic necrosis.[3,17] The previous studies by Komolafe et al., and Deherkar et al., have highlighted prognostic value of elevated CRP values in assessment during early stages of AP.[17,18] Stirling et al., suggested that rise of >90 mg/dL or value of >190 mg/dL at 48 h can prognosticate disease severity with greatest presion.[19] However, American College of Gastroenterology has issued guidelines suggesting that "no laboratory test, including CRP, is practically available or consistently accurate to predict severity in patients with AP" as CRP takes 72 h to become accurate to predict disease severity.[20,21]

In the present study, mild, moderate, and severe mCTSI scores were obtained in 17.78%, 66.67%, and 15.55% patients, respectively. Mortality was observed around 40% patients with severe mCTSI score and significant association was reflected between mCTSI scores and clinical outcome. The findings are in accordance with the observations by Mortele et al.,[5] in which the severity of pancreatitis had significant correlation with the development of organ failure on using mCTSI as compared to CT severity index.

The present study revealed significant positive correlation between CRP values and mCTSI scores in AP patients. The findings are consistent with the study by Irshad et al.,[22] and Banday et al., also suggested mCTSI to be a simple and accurate scoring tool as compared to Balthazr CT severity index and mCTSI to have a significant correlation with clinical outcomes in terms of duration of hospitalization, development of complications, and overall mortality.[6] However a systematic and meta-analysis of diagnostic accuracy studies have concluded magnetic resonance imaging (MRI) to be more specific, sensitive and accurate as compared to CT.[23] MRI has higher recognition ability for diagnosis of pancreatic injury in terms of peripancreatic effusion, pancreatic contour, and vascular proliferation at site of lesion.[24,25]

Despite advances in diagnosis and management, CRP and mCTSI scores have their predictive value in risk stratification and aid in management.

Limitations of the study

The sample size of the present study was limited to 90. The recruitment of the patients for the study was based on non-probability sampling. Although easily accessible,

Table 3: Association of CRP values and mCTSI scores with the clinical outcome in patients with acute pancreatitis

Variable	Categories	Total	Outcome		P-value
			Discharge	Death	
CRP (mg/dL)	<10	4	4	0	0.00002*
	10–21	74	73	1	
	>21	12	7	5	
mCTSI score	Mild	16	16	0	0.000001*
	Moderate	60	60	0	
	Severe	14	8	6	

mCTSI: Modified computed tomography severity index, CRP: C-reactive protein, *P<0.05, statistically significant

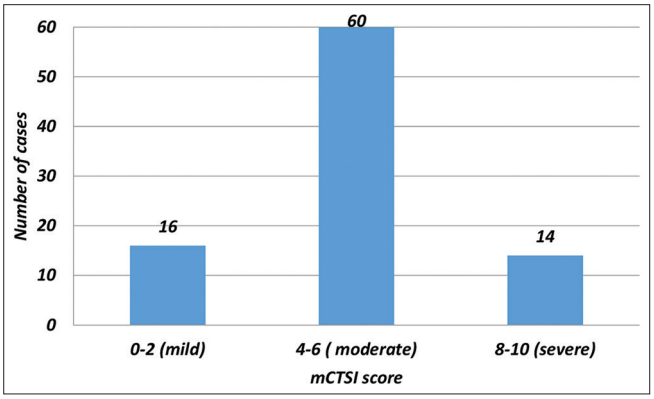

Figure 3: Modified computed tomography severity index scores in patients with acute pancreatitis

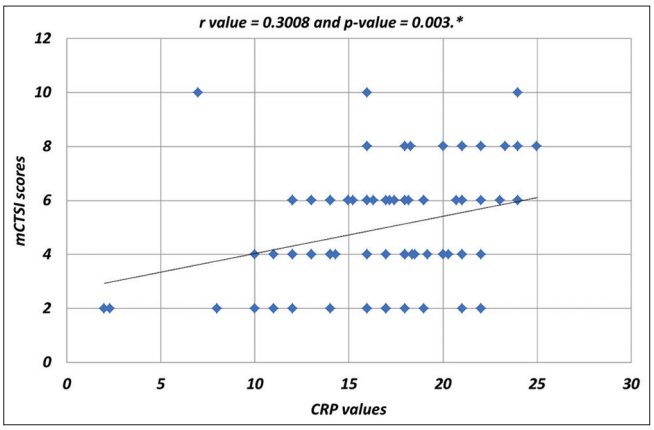

Figure 4: Scatter diagram showing correlation between C-reactive protein values and modified computed tomography severity index scores in patients with acute pancreatitis. r-value–Pearson's coeffient, *P<0.05, statistically significant

it fails to represent general population and has the chance of selection bias. Hence, larger sample size with better sampling techniques can be used to draw conclusions which can be extrapolated to general population.

CONCLUSION

AP demands early diagnosis and interventions. Patients with higher CRP values and severe mCTSI scores had worse clinical outcomes. Furthermore, CRP levels had significant positive correlation with mCTSI scores in AP. Thus, both have the potential of being significant diagnostic and prognostic biomarkers in AP and can be used for better management and positive outcome in AP patients.

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KL- Concept and design of the study, investigation, and statistical analysis, review of literature and preparation of first draft; **NS-** Concept and design of the study, co-ordination, and revision of manuscript; **ABT-** Co-ordination, investigation, and preparation of manuscript; **RB-** Co-ordination, investigation, and preparation of manuscript; **HKG-** Statistical analysis, interpretation of the results, review of literature, preparation of manuscript, and revision of the manuscript; **DRV-** Concept and design of the study, co-ordination, statistical analysis, interpretation of the results, and revision of the manuscript.

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