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ORIGINAL RESEARCH

CRP level as predictor of severity of acute pancreatitis

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ABSTRACT

Introduction: Acute pancreatitis is a potentially fatal disease. Severe acute pancreatitis can result in complications like multiple organ failure and even death. The study was conducted to know the usefulness of CRP levels as a gauge for acute pancreatitis severity. **Aim:** To study relation of CRP level as predictor severity of acute pancreatitis. **Patient & methods:** A size of 60 patients meeting inclusion criteria was taken for study. C reactive protein was done at the time of admission by standard method and was compared with modified CT severity index. **Results:** Patients with higher levels of CRP had higher modified CT severity index. The association was statistically significant ($P<0.05$). **Conclusion:** CRP being simple, cheaper and easily available can be used as a tool in early detection of severity of acute pancreatitis and further treatment planning in these patients.

Keywords: CRP, Modified CTSI, Acute pancreatitis

INTRODUCTION

Abdominal discomfort with abrupt onset and systemic inflammation are the hallmarks of acute pancreatitis (AP), a potentially fatal inflammatory pancreatitis. Severe occurrences of AP can result in complications like multiple organ failure, pancreatic necrosis, and even death, however the majority of cases are moderate and self-limiting. Accurately estimating the severity of AP in advance is essential for effective treatment and bettering patient outcomes.

The characteristic of the frequent illness known as acute pancreatitis is immediate inflammation of the pancreas. The severity of acute pancreatitis can vary widely, ranging from mild cases that need conservative management to severe, complicated conditions with high rates of morbidity & mortality. Two main categories are used by the Atlanta classification to categorize acute pancreatitis. [1] These are:

- The acute inflammation of the pancreatic parenchyma and surrounding peri-pancreatic tissue is a characteristic of interstitial edematous acute pancreatitis.
- The necrosis of the peri-pancreatic and pancreatic parenchyma is a characteristic of necrotizing acute pancreatitis.

The following categories of acute pancreatitis are distinguished based on the severity of the illness:

- In mild acute pancreatitis, there is the absence of local or systemic complications and organ failure.
- In moderately severe acute pancreatitis are local complications with or without organic failure for less than 48 hours.
- In severe acute pancreatitis, there is persistent organ failure for more than 48 hours with the involvement of one or more than one organs.

There are several causes of acute pancreatitis, such as hypertriglyceridemia, gallstones, and alcohol consumption. Geographical and social factors influence etiologies. Hypertriglyceridemia, alcohol, gallstones, drug-induced pancreatitis, and idiopathic instances are common causes. Post-procedural problems, autoimmune diseases, bacterial and viral infections, trauma, congenital abnormalities, genetic disorders, hypercalcemia, parasite infections, renal disease, toxin exposure, and vasculitis are additional risk factors. [2]

The liver produces C-reactive protein (CRP), an acute-phase reactant, in reaction to inflammation, infection, or tissue damage. Its levels can be used to determine how severe a number of inflammatory disorders, such as acute pancreatitis, are. CRP is a pentameric polypeptide of 206 amino acids that is a

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member of the pentraxin 1 family, which is a short pentraxin family. Interleukin-6 (IL-6) is the main factor that stimulates the synthesis of CRP, which is mostly produced in the liver's right lobe. From a physiological standpoint, CRP is essential for improving cell-mediated immunity because it promotes phagocytosis, speeds up chemotaxis, and activates platelets. CRP levels in healthy persons normally fall between 0.8 and 3.0 mg/L. Acute pancreatitis is frequently accompanied by elevated CRP values, which indicate the severity of the inflammatory response to the illness. [3,4]

This study investigates the usefulness of CRP levels as a gauge for acute pancreatitis severity. This study aims to assess the relationship between CRP levels and the severity of acute pancreatitis by reviewing the literature that has already been written, examining clinical data, and doing the necessary statistical analysis. Comprehending the function of CRP in forecasting the severity of AP may have noteworthy clinical consequences, supporting medical professionals in risk assessment, treatment plan selection, and prognosis. In the end, this study's findings might help patients with acute pancreatitis receive better care and have better results.

MATERIALS AND METHOD

Study Design

Type of study: Prospective observational Study

Study Period: The study was conducted over a time period of 18 months.

Study Area: The study was conducted in SGRRIM&HS, Dehradun

Study Unit: All patients fitting the inclusion criteria were included in the study.

Sampling technique:
All eligible patients admitted in the department of surgery/medicine for acute episode of pancreatitis

Selection of subjects:
Inclusion criteria:
1) Acute episode of Pancreatitis.

Exclusion criteria:
1) Chronic pancreatitis
2) Patients with disorders like rheumatoid arthritis, coronary artery disease, diabetes mellitus,Obesity etc., which increase serum CRP levels were excluded from the study.

STUDY PLANNING:-
Diagnostic criteria:-[5]
Acute Pancreatitis was diagnosed if a patient had more than two of the three following findings:
1) Typical abdominal pain of Acute Pancreatitis (acute onset of a persistent and severe epigastric pain often radiating to the back),
2) Biochemical confirmation of Elevation of serum amylase and/or lipase levels above three times upper normal limit, and
3) Radiological investigation including USG abdomen and CT abdomen with findings suggestive of pancreatitis.

C reactive protein value was done at the time of admission by standard method and was compared with modified CT severity index which was assessed from contrast enhanced CT

Study Tools
Structured case reporting form was used to generate data.

Study Protocol:
1) Patients diagnosed as per above Diagnostic, Inclusion and Exclusion criteria were included.
2) The study was described to the participants as an investigation of management and outcome of their condition and their written consent to participate in the research was sought. After the informed consent, the demographic information was recorded on the data collection form.
3) All patients diagnosed as Acute Pancreatitis were treated with care as per the standard protocol and no additional intervention was done for the study purpose.
4) Rest of the treatment was done as per standard protocol.

The patients were then compared on the basis of clinical and laboratory data collected using standard statistical methods. Data was recorded on a structured case reporting form. Severity was assessed using the modified CT Severity Index.

Data Management and Statistical analysis
The data entry was done in the Microsoft EXCEL spreadsheet and all data was analysed with SPSS software (version 23). Descriptive statistics, such as means, standard deviations, frequencies, and percentages, were calculated to summarize the data. Inferential statistics, such as Student t test, chi-square test and Pearson's correlation coefficient were used to identify associations between variables. For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS

The present study was conducted on 60 patients with acute pancreatitis.

Table 1: Age distribution of study subjects

Age group (years)	Frequency (n)	Percentage (%)
<40	29	48.3
40-60	18	30.0

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>60	13	21.7
Total	60	100

- Most of the patients were <40 years of age (48.3%).
- 30% patients were in the age group of 40 – 60 years
- 21.7% were >60 years of age.

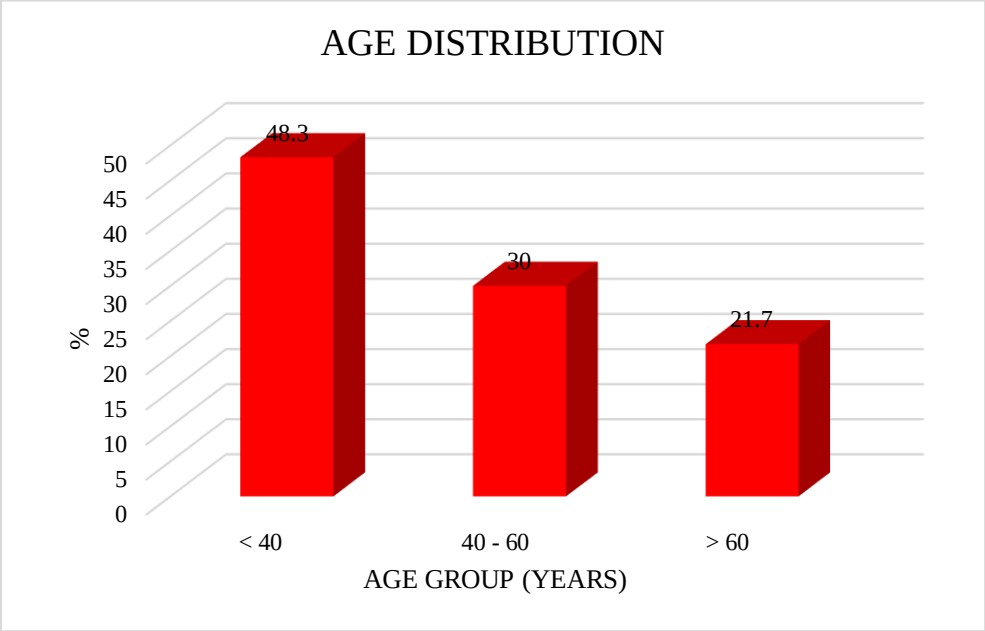

Table 2: Gender wise distribution of the study subjects

Gender	Frequency (n)	Percentage (%)
Female	16	26.7
Male	44	73.3
Total	60	100

73.3% patients were males while 26.7% were females.

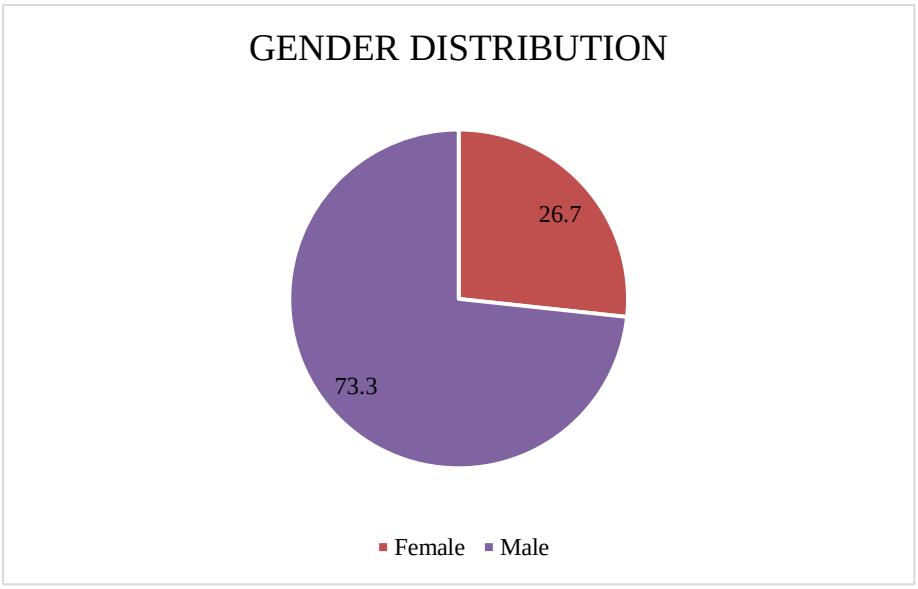

Table 3: Distribution of the study subjects with respect to History of Alcohol Intake

H/O Alcohol Intake	Frequency (n)	Percentage (%)
No	30	50.0
Yes	30	50.0

50% of the patients had history of alcohol intake.

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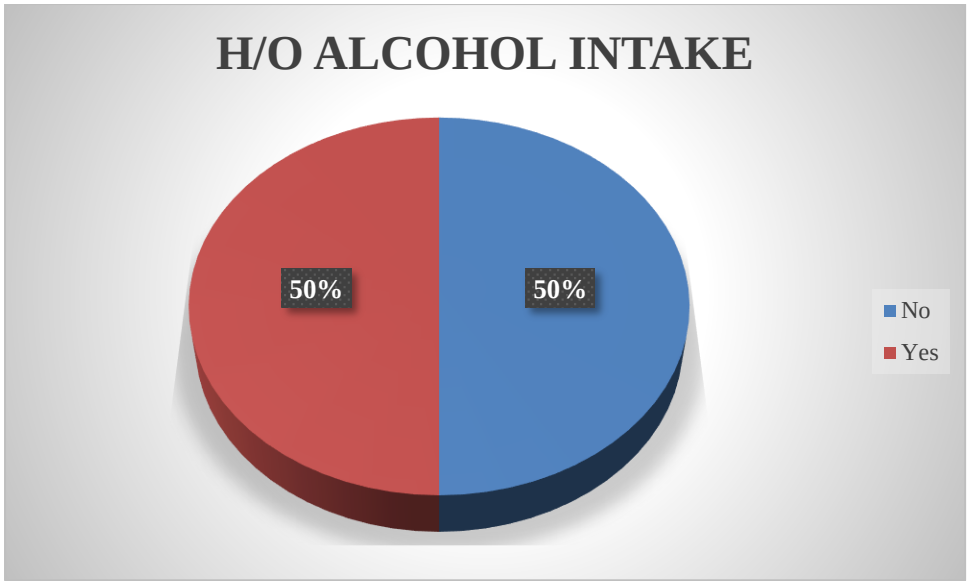

Table 4: Distribution of the study subjects with respect to History of Cholelithiasis

H/O Cholelithiasis	Frequency (n)	Percentage (%)
No	31	51.7
Yes	29	48.3

48.3% patients were found to have cholelithiasis while 51.7% did not have cholelithiasis.

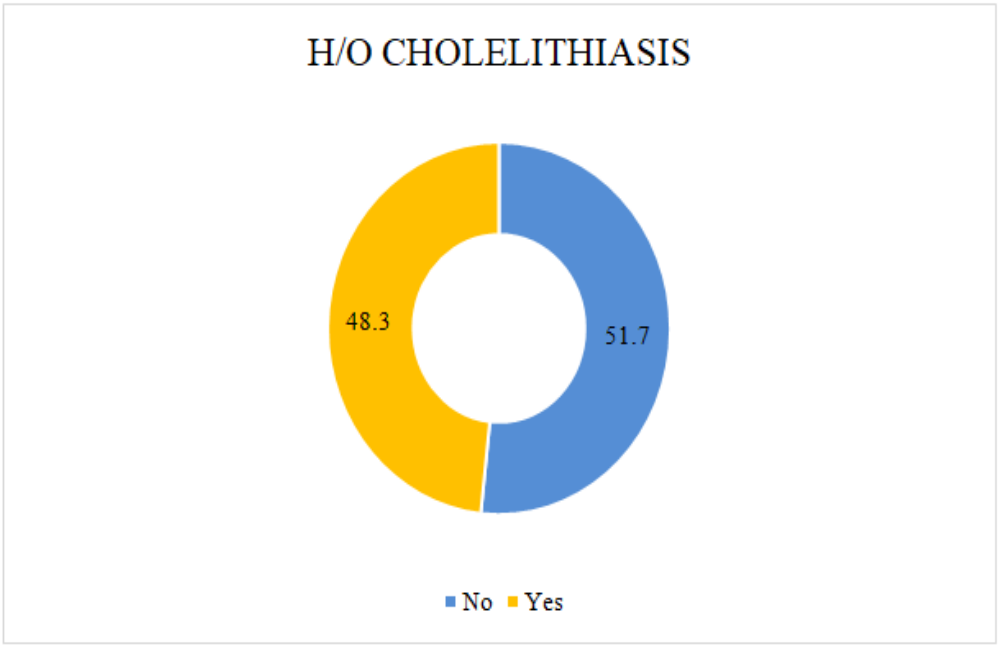

Table 5: Laboratory investigations

Parameters	Minimum	Maximum	Mean ± SD
Hemoglobin	7.6	17.5	13.04 ± 2.29
TLC	3800	39700	13229.50 ± 5880.78
Platelet	21000	583000	200366.67 ± 111138.63
S. Bil(Total)	0.31	22.20	2.55 ± 1.86
S.Bil(Direct)	0.1	19.6	1.74 ± 1.41
SGOT	21	732	91.17 ± 63.66
SGPT	7	678	88.90 ± 71.39
ALP	37	889	156.97 ± 131.93
GGT	21	1337	242.60 ± 226.78

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CRP	7.02	844.1	198.79 ± 151.02
S. Amylase	47	3366	715.12 ± 704.20
S. Lipase	55	24464	4946.73 ± 3397.17
CTSI	2	10	6.78 ± 2.34

The mean hemoglobin level of the patients was 13.04 ± 2.29 g/dL. The mean S. Amylase and S.Lipase were 715.12 ± 704.20 U/L and 4946.73 ± 3397.17 U/L respectively. The modified CT severity index ranged from 2 to 10 with the mean of 6.78 ± 2.34.

Table 6: Correlation Between modified CT Severity Index and CRP

mCTSI (Mean ± SD)	CRP (Mean ± SD)	Pearson's correlation coefficient (r)	p value*
6.78 ± 2.34	198.79 ± 151.02	0.467	<0.0001

A moderate positive correlation (r = 0.467) was observed between mCTSI and CRP using Pearson's Correlation Analysis, which was statistically significant (p <0.0001). This means that higher mCTSI was associated with higher CRP levels.

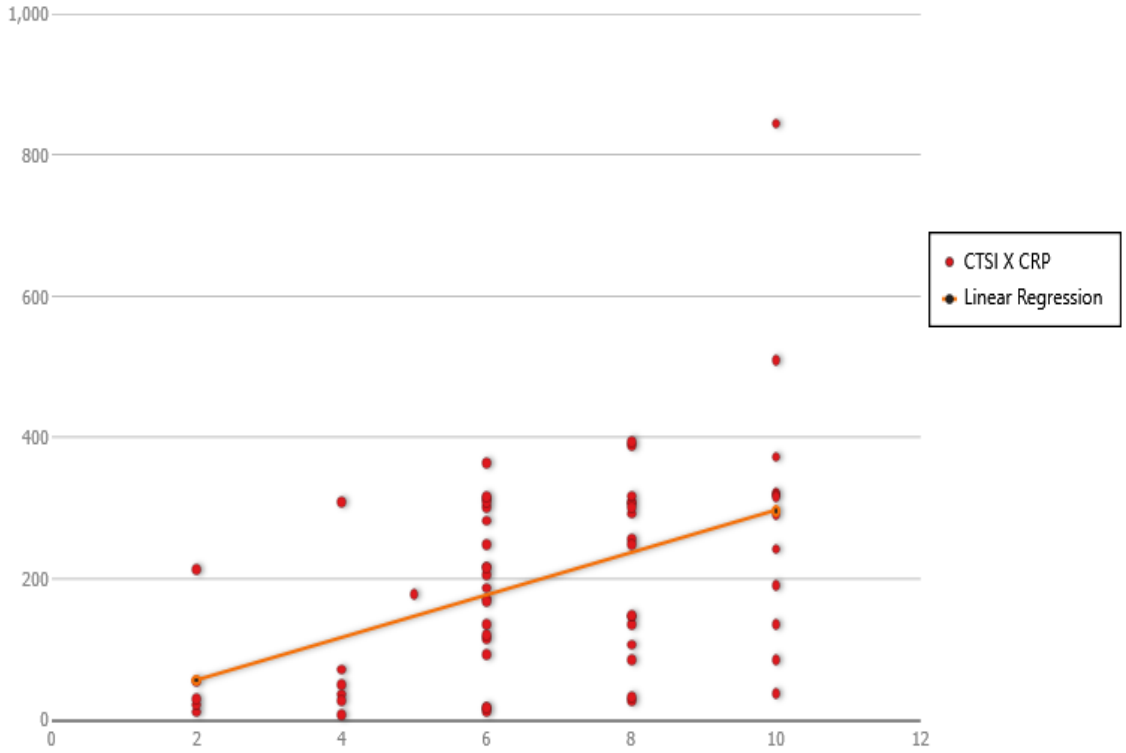

Table 7: Association of mCTSI with CRP levels

mCTSI	CRP		Frequency (n)	p-value*
	Mean	SD		
Mild	65.19	83.81	5	0.009
Moderate	165.43	113.21	27	
Severe	254.80	169.65	28	

- Patients with higher modified CT Severity Index had higher levels of CRP.
  - 5 patients with mild mCTSI have mean CRP level of 65.19 ± 83.81,
  - 27 patients with moderate mCTSI have mean CRP level of 165.43 ± 113.21 &
  - 28 patients with severe mCTSI have mean CRP level of 254.80 ± 169.65
- Using Kruskal Wallis Test this association was statistically significant (p <0.05).

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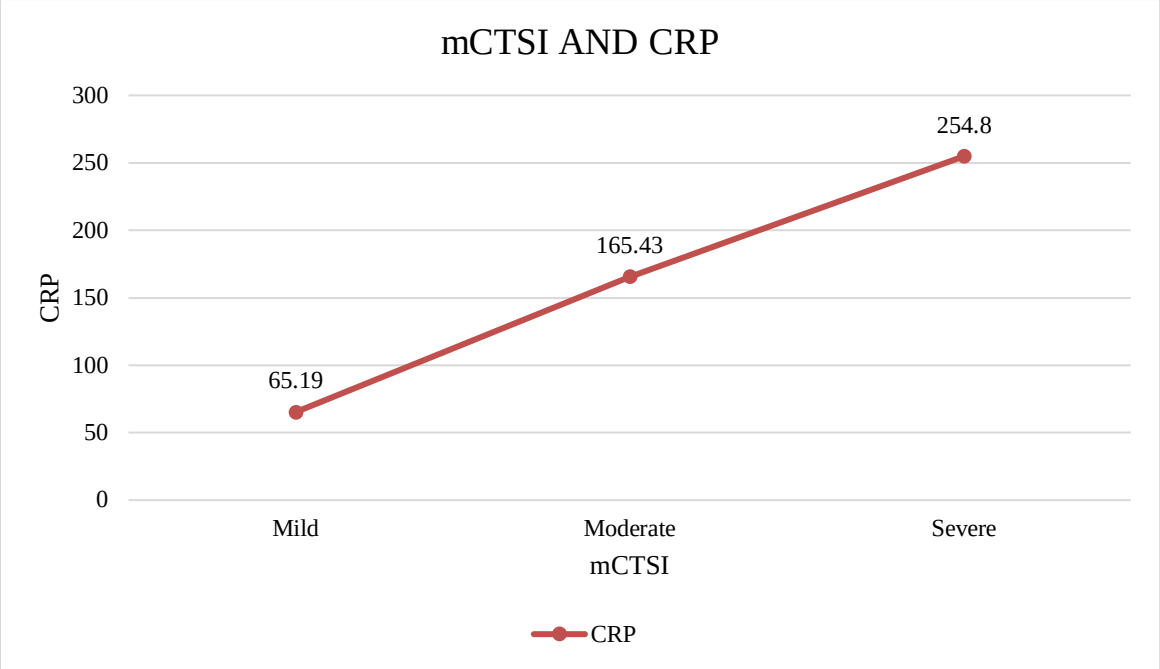
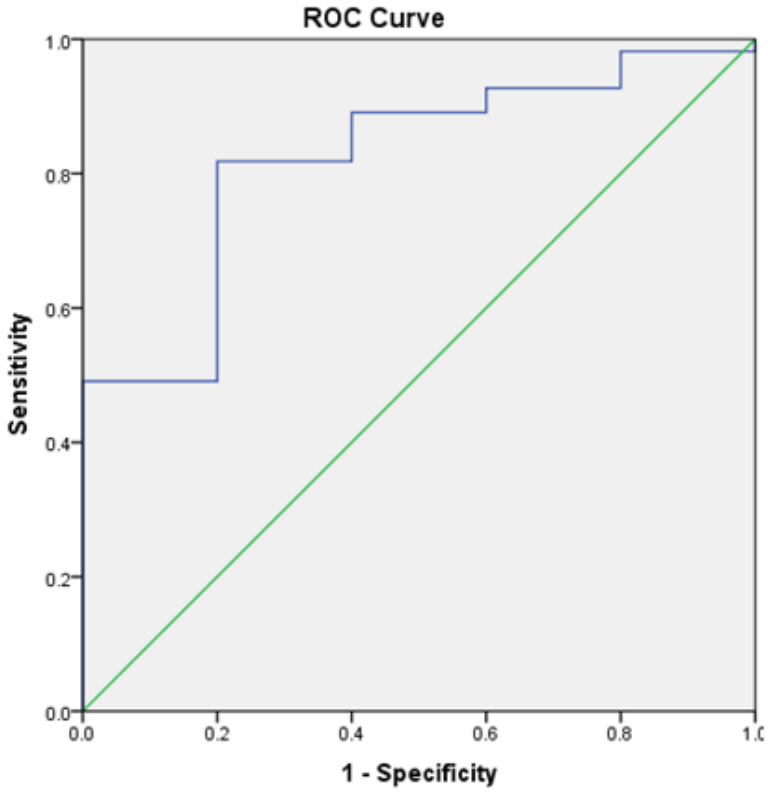


Table 8: CRP as Predictor of mCTSI

mCTSI	AUC	CRP			95% Confidence Interval	
		Cut-off value	Sensitivity	Specificity	Lower Bound	Upper Bound
Mild to Moderate	0.822	61.95	81%	80%	.654	.990
Moderate to severe	0.704	187.6	64%	63%	.573	.835

CRP was a good predictor of mCTSI with AUC-

- For predicting mild to moderate severity as 0.822 and
- For predicting moderate to severe severity as 0.704.



ROC Curve for Mild to Moderate mCTSI

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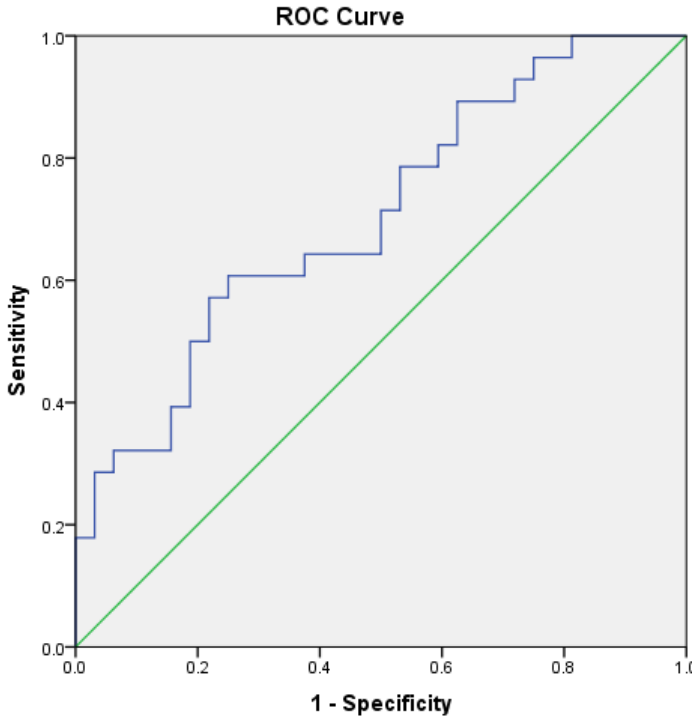

ROC Curve for Moderate to Severe mCTSI

DISCUSSION

In order to determine whether CRP levels may be used as a predictor of pancreatitis severity, a prospective observational study was conducted at SMIH, dehradun hospital with 60 patients who had acute pancreatitis.

Del et al. proposed that prompt diagnosis is essentail for effective therapy and that the most popular scoring systems for acute pancreatitis are sometimes complicated and challenging to apply in clinical settings due to their multidimensional nature[6]. Therefore, the number of uni-factorial prognostic indices of which CRP is the one to estimate has been used in ordinary hospital practice. Although both CRP and Serum phospholipase A2 measurements are useful in determining the severity of acute pancreatitis early on, the CRP test is far simpler to include into regular hos pital procedures. CRP was suggested as a single reference parameter of pancreatic necrosis in the **Schütte et al study** because it can be measured using an easily accessible, low-cost laboratory test and has a good predictive value in a clinical scenario[7].

In the present study Most of the patients were <40 years of age (48.3%). 30% patients were in the age group of 40 – 60 years and 21.7% were >60 years of age. 73.3% patients were males while 26.7% were females. **A study conducted lahan et al (2023)**[8] by Among 90 patients with diagnosis of AP, majority were males [n=81 (90%)] Among 90 patients with diagnosis of AP, majority were males [n=81 (90%)]. The mean age of the participants is 36.94±9.19 years, with majority (40%) in the age group of 31–40 years. **Another study conducted by sethi et al (2021)** [9]. In this study group (n=60), there were 41 males and 19 females with M: F ratio=2**. Another study conducted by hebbar et al (2023)**[13]**.** The study was conducted on 50 patients to know the role of c-reactive protein in severity stratification of acute pancreatitis. It was observed that mean age of the patients was 42.82±12.29 (18- 65) years. Majority of the patients (52%) were male while females were only 48%. **Another study conducted by Raghuwanshi et al (2016)[14]**, Study was undertaken to evaluate the acute pancreatitis on CT and the patient was prognostically correlated on the basis of CTSI (including Balthazar's Computed Tomography Severity Index and the Modified Computed Tomography Severity Index). The study group consisted of 35 male and 15 female patients with a male: female sex ratio of 2:1. **In a prospective study by Block et al.**, consisted of 61 (65.6%) males and 32 (34.4%) females with a male to female ratio of 2:1 [15]. **Silverstein et al.**, in his prospective study of 102 patients, also had a male to female ratio of 2:1 [16]. **Similar study conducted by Irshad et al (2021)**[17]. In this study 59.7% were males and remaining were females. Similarly **Wang Y et al** [18] found 51.64% males and 48.36% females. While inconsistently **Kayar Y et al** [19] reported that out of all study participants 111 were females and 69 were males. According to the study, men were more likely to have AP and its related co-morbidities. Our findings agreed with those of the earlier research.

In the present study 50% of the patients had history of alcohol intake. **A study conducted lahan et al (2023)**[8], Alcohol consumption was present in 91.11%(n=82) of the patients of which 82.22% (n=74) consumed more than 50 g/day. **Another study**

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conducted by sethi et al (2021)[9], the most common cause of acute pancreatitis in study was alcohol abuse, seen in 27 patients (45%)**. Another study conducted by hebbar et al (2023)**[13] ,the study observed that pain (96%), vomiting (60%), abdominal distention (18%), and jaundice (18%) was the most common presenting symptoms. It was observed that 72% patients were consuming alcohol, and there were 42% smokers while 40% patients had both habits. Alcohol was the most common cause of acute pancreatitis as it was seen in 72% of the study population.

In the present study 48.3% patients were found to have cholelithiasis while 51.7% did not have cholelithiasis. **Another study conducted by sethi et al (2021)**[9] in 11 patients, acute pancreatitis was associated with biliary calculi and in 2 patients, trauma was the etiological factor for pancreatitis.

In this study, alcohol was the most common cause of AP, occurring in 50% of the study population, while biliary causes of pancreatitis were only observed in 48.3%. This is in contrast to **Roberts et al [10]** UK based report from 36.9% of patients, which stated that gallstones were the most common cause of AP, followed by alcohol (22.0%). Parallel findings to the current study were found in investigations by **Sekimoto et al [11]** and **Abbasi et al [12]** that in the Japanese population, alcohol was the primary cause of 53% of cases of AP, with the Biliary system accounting for 20% of cases. This study supports the body of evidence that indicates the most frequent causes of pancreatitis are gallstones and alcohol.

In the present study, 5 patients with mild mCTSI have mean CRP level of 65.19 ± 83.81, 27 patients with moderate mCTSI have mean CRP level of 165.43 ± 113.21 & 28 patients with severe mCTSI have mean CRP level of 254.80 ± 169.65. Patients with higher modified CT Severity Index had higher levels of CRP and this association was statistically significant ($p < 0.05$). In AP patients, the current study found a significant positive connection between mCTSI and CRP readings. According to research by **Alfonso et al. [20]** and **Cardoso et al. [21],** who used CRP values of 200mg/dl and 170mg/dl respectively, to predict SAP and necrotizing pancreatitis, it may be concluded that there was a substantial correlation between CRP and pancreatitis severity. The CRP cut off of 150mg/dl, which is recommended by **Wilson et al. [22]** findings and the UK recommendations for the management of AP[23], is also achieved by this study. Therefore, this study demonstrates that in terms of predicting SAP, a CRP of >150mg/dl is just as diagnostic as higher values. The results align with the research conducted by **Irshad et al. [17]** and **Banday et al**. [24], which proposed that mCTSI is a straightforward and precise scoring instrument when compared to the Balthazar CT severity index. Additionally, the study found a noteworthy correlation between mCTSI and clinical outcomes, including hospitalization duration, development of complications, and overall mortality.

In the present study, CRP was a good predictor of CTSI with AUC for predicting mild to moderate severity as 0.822 and for predicting moderate to severe severity as 0.704. **Contrary to our results, in a study conducted by Ahmad et al (2021)** [25] CRP at admission showed low discriminatory value (AUC= 0.54, p-value= 0.74). Similar results have been reported by **Fisic et al** who have reported the AUC 0.51 for the CRP measured on the first day [26]. **Ke et al** reported an AUC of 0.67 for day 1 CRP in the prediction of critical acute pancreatitis [27]. In current study, CRP at admission had AUC of 0.822 for predicting mild to moderate pancreatitis and 0.704 for predicting moderate to severe pancreatitis. This is approximately in accordance to other studies that have reported values in the range of 0.84 to 0.90 [28, 29].

LIMITATION OF THE STUDY

The empirical results reported herein should be considered in the light of some limitations:

- The study's sample size was restricted to 60 patients. The study included all eligible patients admitted to the medicine or surgical department due to an acute pancreatitis episode. It is easily available, yet it does not accurately reflect the population as a whole. Therefore, conclusions that can be applied to the entire population can be made with a larger sample size.
- As our centre is a tertiary Care centre therefore there might be Delay in presentation to the hospital as the patients seek over the counter medications or complementary and alternative forms of medicine for the most common symptom of abdominal pain or it could be that of a referral bias.
- Since CRP is a non-specific indicator of inflammation, patients with elevated CRP may only be excluded by a comprehensive history and questionnaire; nevertheless, subclinical inflammatory disorders that elevate blood CRP levels cannot be ruled out.
- Due to technical and financial constraints, elaborate investigations to exclude hematological and rheumatologic disorders were not done.

CONCLUSION

The following conclusion were extracted from the study:

- A moderate positive correlation was identified between the modified CT Severity Index and CRP levels, suggesting higher inflammation markers are associated with increased severity in CT scans. CRP levels and mCTSI scores showed a significant positive correlation. As a result, both may serve as important biomarkers for diagnosis and prognosis in AP and can be applied to improve patient care and outcomes.
- A significant relationship was observed between the severity of CT findings and CRP levels,

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indicating that higher CRP levels is associated with greater severity. Thus, CRP levels at the time of admission could be used to detect severity of acute pancreatitis which in turn could help to improve patient outcome by early detection of severity and accordingly planning the further course of treatment

- CRP levels were predictive of the severity of CT findings, with the area under the curve indicating reasonable predictability for differentiating between severity levels. Since not all patients with acute pancreatitis can have a CT examination. For instance, patients with renal failure are unable to undergo a contrast-enhanced CT study and also there might be some financial constraints to the patient in undergoing contrast enhanced CT study. So, CRP being cheaper and easily available can be used as a tool in early detection and treatment planning in these types of patients

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