



## **A Study on C-Reactive Protein Levels in Pancreatic Diseases and Its Prognostic Significance**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i37A32006

Editor(s):

(1) Dr. Rafik Karaman, Al-Quds University, Palestine.

Reviewers:

(1) D K Prajapati, Gajra Raja Medical College, India.

(2) Waqas Alam, Abdul Wali Khan University Mardan, Pakistan.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/71219>

**Study Protocol**

**Received 10 May 2021**  
**Accepted 14 July 2021**  
**Published 15 July 2021**

### **ABSTRACT**

**Background:** Pancreatic diseases are one of the most prevalent challenges faced by surgeons throughout their work. Unless and until surgery is noted for its complications, the most traditional management line has always been conservative. As a diagnostic tool for it, amylase and lipase have been used to date, but some prognostic methods such as CRP are being used in this research, assessing its importance as a prognostic tool

**Objectives:**

1. To measure levels of CRP in patients of pancreatic diseases and evaluating if CRP concentrations expect the magnitude of the disease.
2. To assess the accuracy levels of CRP in diagnosing pancreatic diseases by assessing with CT diagnosing.
3. To find out correlation between levels of C-reactive protein and CT findings in pancreatic diseases.

**Methodology:** It is a prospective observational study completed on the patients of pancreatic diseases. It will be conducted at Surgery Department, JNMC and AVBRH, Sawangi (Meghe), DMIMS Wardha (DU).

**Results:** The result would be undertaken in SPSS software

**Conclusion:** Conclusion will be based on findings for study of protocol

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**Keywords:** C - reactive protein (CRP); pancreatic disorders.

## 1. INTRODUCTION

In India pancreatic diseases, has been significant cause of morbidity and mortality and elsewhere. With an increasing incidence in alcoholism and biliary diseases, the Pancreatitis incidence is expected to increase as a major etiological factor.(1) Pancreatic diseases is known to man from pre-Christ periods as the Alexander the Great's, death at the age of 33 years (356 323 BC) is attributed to acute narcotization -pancreatitis secondary to his pathological alcoholism. In the 17th century, Wirsungin and early 19th century Halstedon performed detailed research on the organ and the state of this disease.

Early descriptions of pancreatic diseases were based on the biliary etiology classically described by Opie in his paper in 1900 where in he proposed the Common channel theory [1].

In 1925, Moynihan made the classical statement- "PANCREATIC DISEASES SPECIFICALLY ACUTE PANCREATIC CONDITIONS". It's the most dreadful of overy diseases that develop in association with viscera of the abdomen. The abrupt onset, the limitless suffering that occurs with it and the mortality that accompanies it, make it the most formidable of all the disasters [2].

In 1974, Ramson was the first to develop a risk stratification rating system for acute pancreatitis patients and to measure mortality and morbidity for each individual case [3]. Early surgery was the rule in pancreatic diseases till 1970s. Trapnell after extensive studies published paper in 1967 describing early surgery to be positively harmful and should be avoided [3]. This was later on confirmed by Ranson [4].

In clinical appearance and severity, acute pancreatitis is extremely variable. The seriousness of this illness is dependent on both anatomical and physiological parameters. A grading system for severity was created by Balthazar and Ranson based on CT performance. By evaluating the grade of pancreatic and peri-pancreatic swelling, liquid assortment and parenchyma necrosis, this computed tomography severity index (CTSI) is useful. The best-established and most available redness marker is the critical phase reactant C-reactive protein (CRP). Most pancreatic

pathology patients have minor disease and their medical indications and test results are resolved within 3 to 5 days with supportive treatment. Extreme pancreatitis, on the other hand, is allied by multiple structure failure and local problems such as necrosis, abscess development and pseudo-cysts, and accounts for 15-20% of these instances. Twenty-eight percent of our cases were complex but, in the mainstream of patients, the ailment was self-restrictive. Numerous grading classifications are used for expecting the sternness.

The precise pathogenesis of AP remains elusive, despite intensive analysis over centuries. While there have been several hypotheses suggested, none of them seem to be complete. Some of the proposals include the popular pathway theory of atypical biliopancreatic duct, the model of pancreatic autodigestion, the concept of gallstone migration, the philosophy of enzyme activation, the concept of kinin and complement instigation, the scheme of microcirculation trouble, and the theory of pancreatic acinar cell programmed cell death and necrosis, wholly of which are however debatable. Because of particular etiologies, they may only clarify certain aspects of pathogenesis or fit disorder. In the study of AP pathogenesis, the biggest challenge is its speedy progression and virtual remoteness of pancreatic tissue. To solve this issue, researchers have nowadays used animal replicas to learn the molecular facets of a pancreatic pathogenesis. The paradoxical findings of pathogenesis, gained from various animals subjected to analogous etiology, further complicate the issue. The most widely accepted hypothesis is the untimely stimulation of trypsin in pancreatic parenchyma, which serves as the vital footstep in inducing pancreatic tissue autodigestion and succeeding limited and general inflammation. The sickness expansion can be seen as a three-phase cycle irrespective of the originating incident: local inflammation of the pancreas and a systemic provocative retort accompanied by the ultimate point of multi-organ dysfunction.

In addition, etiology does not influence CRP levels, thus demonstrating that unfluctuating scientific results are autonomous of etiology. Equally CRP and CTSI were able to foresee indisposition and death in the assessment of scoring systems in outcome prediction of pancreatic illness. In a study investigating the

worth of C-reactive protein purposes in assessing the harshness of acute pancreatitis and the association of CRP with serum phospholipase A2 action and experimental standing, CRP and S-phospholipase A2 strength were found to be useful in the primary valuation of acute pancreatitis severity, but the CRP assay is much informal to embrace in clinic schedule. Lipoprotein a, SAA, TAP, poly-C avid ribonuclease, urinary trypsinogen activator, matrix metalloproteinase 9, macrophage-migration inhibitory factor, PMN etc. are other markers under evaluation.

The very fact that further investigates endures for a restored prognosticator means that the most reliable measure might not be serum CRP. CRP is conveniently available before a more reliable predictor comes along. If single estimates are predictive, they will prove to be even more cost efficient. hence, this analysis uses only a single estimate of CRP. And if improved pointer comes along, the locus constraint by which the extra will be umpired will always be CRP. The benchmark for radiological verdict of acute pancreatitis is CT-scan abdomen with IV comparison, as shown by Balthazar and colleagues. The incidence of acute pancreatitis and pancreatic necrosis has been shown to be predictive. A high computed tomography value and a CRP rate more than 150 mg/dl on ICU admission were found by Makela et al to be useful in guessing mortality. Male patients with elevated CRP, respiratory and renal failure have a lengthier stay in the ICU.

The rest of the initial studies on pancreatic illness were dependent on biliary pathology. Later, though on alcoholism was found To be a big etiological agent especially in males. Geographical variations are noted in the etiological factors described with most of the recent European studies show biliary pathology to be predominant compared to the Asian studies show alcohol as the more significant etiological factor. Serological evaluation of lipase and amylase is becoming the gold standard for confirming pancreatic illness. Even though many extensive and complicated scoring systems have come, Ranson's scoring system is still the easiest and is most commonly followed. Conservative management has become the touchstone for the supervision of these pathologies. Surgery has a minimal role in acute disease and only in cases of bilio-pancreatic pathology, infected pancreatic necrosis and

abscess formation. Mortality in general has reduced after the institution of early confirmatory techniques and effective conservative management. This condition is familiar for its recurrence and significant number of abdominal complications, such as ascites, pseudocyst, necrosis, abscess, venous thrombosis and aneurysms, and intestinal complications, which may require surgery. One of the major causes of acute pain in the abdomen is acute pancreatitis. The variation has been noted in its clinical presentation. No complications were seen in most of the patients recovered from it. However; in some patients the complications like pancreatic ascites and necrosis have been noted, which are severe in nature; and high mortality and morbidity is noted in these patients. The disorder is mild in most patients, and resolves spontaneously, but some patients present with a florid and rapidly deteriorating inflammatory process. Significant morbidity and mortality ranging from 30% and 50% are correlated with extended hospitalization.. The pathogenic mechanism causes the auto-digestion of pancreas and an intense Immune system-interposed inflammatory response, which is done via the zymogens activation synthesized by pancreas. The inflammatory reaction may be restricted to the pancreas or may advancement to a systemic inflammatory response syndrome (SIRS). The immune response does not depend on the instigating factor but is responsible for most of the subsequent damage. A detailed understanding of the pathogenic mechanisms is essential to facilitate early and effective intervention in severe pancreatitis which has high morbidity and mortality. However, means of identifying which particular case will develop a severe variety of acute pancreatitis have been lacking. Various clinical, biochemical and imaging criteria has been suggested as predictors of seriousness of pancreatic pathologies. There has been a deficiency in the character of analytical pointers (pancreatic enzymes such as amylase and lipase) as extrapolative indicators. As prognostic measures, other biochemical markers including C-reactive protein (CRP), pro-calcitonin and the like are underneath assessment. CRP estimation is inexpensive and readily accessible. In this survey, an attempt has been made to see if an efficient predictor of morbidity and mortality is a single and initial estimate of CRP levels in pancreatic disorders. The study is conducted with the aim to evaluate the CRP LEVELS in pancreatic diseases.

## 2. OBJECTIVES

1. To measure levels of CRP in patients of pancreatic diseases and evaluating if CRP concentrations prognosticate the magnitude of the disease.
2. To assess the accuracy levels of CRP in diagnosing pancreatic diseases by assessing with CT diagnosing.
3. To find out association between levels of C-reactive protein and CT findings in pancreatic diseases.  
It will be a Prospective observational study.

## 3. METHODOLOGY

**Design of the study:** Prospective observational Study .

**Population of the study:** Patients with complaints about pancreatic diseases who come to AVBRH.

**Setting:** A.V.B.R.H. Sawangi (Meghe) Wardha.

**Duration of study:** Sept 2020 to Oct 2022

**Sample Size:** 85

### Inclusion criteria:

1. Patients aged between 18-65years with pancreatic diseases characterized by elevated serum amylase and serum lipase.

### Exclusion criteria:

1. All gastrointestinal conditions except pancreatic diseases.
2. Age <18years and >65years.

**Study Protocol:** It is a prospective survey performed on the patients of pancreatic diseases. It will be conducted at Surgery Department, JNMC and Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), DMIMS Wardha.

**SCOPE-** The Study will be useful for establishment of prognostic significance of crp in pancreatic diseases and to know its clinical significance to predict the severity of the disease.

It will bring into attention the simultaneous presence of C-REACTIVE PROTEIN and other inflammatory markers in pancreatic diseases.

## 4. IMPLICATIONS

Our recommendation is that every patient above 18years of age and below 65years of age with pancreatic disorders should be screened for CRP and it may be used as marker for severity of the pancreatic diseases.

CRP does not rule out any circumstances, so CRP is not included in diagnosing the pancreatic diseases, But CRP levels were tested With regard to their capability to guess seriousness, necrosis, complications, mortality, morbidity as an addendum to predict and complications in pancreatic diseases. CRP levels of less than or equal to 200 mg/dl at 72 hours are sufficiently beneficial for ruling out a high standard of likelihood of necrosis in pancreatic diseases.

### 4.1 Methodology

Criteria for inclusion and exclusion will be applied to patients with presentations of pancreatic diseases to the department of surgery, AVBRH. The research will inform patients and only those patients who plan to participate in the study will be included.

Database collection will include Medical history documentation, age, sex, pre-hospital interval, vital signs, alcohol intake with its duration, drug history. Blood will be drawn routinely on arrival of the patient to the department of surgery for Differential count, platelet count, serum amylase and lipase, whole blood count.

CRP level determination will be conducted on the same sample of serum taken for other biochemical studies. The blood drawn will be stored in various vacutainers and marked for various tests accordingly. If there is not sufficient serum to assess the CRP amount, then that sample will be discarded and a new sample will be drawn. The serum sample for estimation of CRP levels will be stored at -70 degree immediately after centrifugation. The sample will be processed only after all collected samples are completed.

## 5. OUTCOME ASSESSMENTS

Once the intervention has been applied, the groups will be followed up and outcomes will be measured to evaluate the values of CRP. Assessment of outcomes will be done at baseline, and at discharge. Serum CRP LEVELS will be sent on day 2 of admission and 2<sup>nd</sup>

sample of CRP will be sent on day before discharge. CECT of the abdomen of the patient will be done 72hours after admission.

### 5.1 Expected Outcome and Result

We expect that we will be able to establish a correlation between C-REACTIVE PROTEIN and pancreatic disorders. We will be able to establish the prognostic significance of CRP in pancreatic disorders. Final results will be obtained after detailed completion of the study.

### 5.2 Analysis Plan

Analysis will be done with the intention of treating values. Both respondents with details available at baseline and follow-up visits will be included. The impact of missing values will be explored in sensitivity analysis. The data will be entered into the Excel spread sheets and statistical analyses will be conducted via SPSS software. Descriptive assessments of age, sex and compliance with care will be done.

## 6. DISCUSSION

CRP is a hepatocyte synthesized acute phase reactant and is commonly raised in inflammatory circumstances [5]. Cytokines alike IL-6 are strong makers of liver crp formation .The serum level of CRP takes about 72hours to peak following the commencement of warning signs [6]. Today it is the most frequently used solo biomarker in AP for seriousness. This is because it is cheap, readily accessible and simple to calculate. As an indicator of severity in AP, a value of more than 150 mg/dL is frequently acknowledged. CRP has a sensitivity of 80-86 percent at this cut-off stage and a specificity of 61-84 percent for analyzing necrotizing pancreatitis within the first 48 hours after symptoms begin [7]. Khanna et al. observed 100 percent sensitivity and 81.4 percent specificity for pancreatic necrosis finding in their study. The late peak (48-72 hours) and its unspecific landscape as an inflammatory marker is the demerit of CRP as a marker. Additional stirring settings such as cholangitis and pneumonia should be lined out prior to CRP calculation.

Trivikraman et. al. cross-sectional study reported CRP levels were found to be in moderate agreement with CT severity index with a sensitivity of 66.7%, specificity of 86.3%, positive predictive value of 64.3% and a negative predictive value of 87.5% and a K score of

0.524.10 Trivikraman et al. cross-sectional study observed on the basis of CRP levels >150, severe pancreatitis was diagnosed in 16% alcoholic pancreatitis, 9% gall stone pancreatitis and 1% each of idiopathic, malignancy and trauma induced pancreatitis [8]. Few of the studies on C - reactive protein were reviewed [9-12]. Studies on beneficial effects of Ghrelin in different situations were reported [13-17].

## 7. CONCLUSION

CRP could be used as prognostic marker in pancreatic diseases and its raised values will determine the severity of the diseases. It can also be compared with serum amylase and serum lipase levels also. It will help to establish the correlation between CRP and CT findings whether the raised CRP values correlate with CT diagnosing findings.

## ETHICAL APPROVAL & CONSENT

Informed consent will be obtained from all patients and previous approval from the DMIMS institutional ethics committee (DU) will be taken.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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