ORIGINAL RESEARCH PAPER

General Surgery

C-REACTIVE PROTEIN AS A RELIABLE PROGNOSTIC MARKER IN PATIENTS WITH PERFORATIVE PERITONITIS : A PROSPECTIVE STUDY

KEY WORDS: C-reactive protein, perforative peritonitis, mortality, survival, prognostic marker

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ABSTRACT

The aims of the study were to find whether an increase in C-reactive protein was a reliable prognostic marker in patients with perforative peritonitis and to determine whether the levels of C-reactive protein had any correlation with the type of perforation.A total of 104 patients with perforative peritonitis presented to Madras Medical College,Rajiv Gandhi Government General Hospital from February 2018 to November 2018 were chosen and allocated into two groups based on the outcome as mortality or survival.88 patients were in the survival group and 16 patients were in the mortality group.the C-reactive protein distribution in both these groups were recorded along with the type of perforation.Data were processed using SPSS software.All values were expressed as mean±standard deviation / median.Comparison of C-reactive protein between the two groups was done using student't'test and prognostic accuracy of the parameters were done using ROC curve analysis.It was found that an increase in C-reactive protein was associated with adverse outcome in perforative peritonitis patients.From this study,we conclude that C-reactive protein is a reliable marker of survival.It allows timely identification of high risk patients and can be used as a marker for risk stratification and hence can be considered a reliable prognostic marker in perforative peritonitis.It can also be concluded that there is no correlation between C-reactive protein and type of perforation.

INTRODUCTION:

Perforative peritonitis is the commonest surgical emergency in India. Inspite of advances in diagnosis,intensive care treatment, surgical techniques and antimicrobial therapy management of perforative peritonitis continues to be challenging for the surgeons.Peritonitis is the commonest cause of sepsis in developing countries. Despite the treatment measures,mortality rates are still high (upto 40%).In addition to this in developing countries, most of the patients present to the clinic late with septicemia,increasing the morbidity and mortality of the disease.This increases the need for a tool predicting the morbidity and mortality in patients with perforative peritonitis.The etiological spectrum of perforative peritonitis in india differs significantly from its western counterparts.It is commonly seen in younger age groups.The site of perforation most commonly involves the proximal part of the gastrointestinal tract whereas it is distal in the western countries.Etiological factors also show a wide geographical variation.In India the most common causes of perforation are peptic ulcer,typhoid followed by appendicular and tubercular perforations.The most important factors responsible for the mortality are Septicaemia and Shock.C-Reactive Protein(CRP) is an acute phase protein which is essential for the host defence against inflammation particularly in infection.The increase is more for bacterial than viral infections [1] .C-Reactive Protein(CRP) starts rising within 6 to 12 hours and peak levels are at 48hours.This promoted us to assess the diagnostic value of C-reactive protein(CRP) as mortality marker in patients with perforative peritonitis [2].

METHODS:

The present study was done in Madras medical college, Rajiv Gandhi Government General Hospital between February 2018 to November 2018. Total of 104 patients with perforative peritonitis presented consecutively to this college were chosen in the study population in the age group of 15-90 years.

Inclusion criteria

Patients with secondary bacterial peritonitis due to hollow viscous perforation (by clinical and radiological methods) were included.

Exclusion criteria

Patients with spontaneous bacterial peritonitis
Malignant perforation,
Traumatic perforation,
Non-resusticable patients,
Post-surgical leak.

Diagnosis of peritonitis due to hollow viscous perforation was done by History and Clinical Examination, X-ray chest PA view showing air under diaphragm, USG abdomen showing free fluid in peritoneum and CT scan.

Mortality was defined as any death occurring during the hospital stay. Morbidity was defined in terms of post-operative complications such as wound infection, Intra-abdominal collection, pneumonia or lung atelectasis, Acute myocardial infarction or heart failure, Acute renal failure and urinary tract infection.

Once the diagnosis of peritonitis was made,the patients were enrolled in the study.In addition to personal data such as name, age, sex other details like comorbid illness,perforation operation interval, heart rate, blood pressure were recorded. Blood samples were to be collected for determination of AEC[3]. Blood samples were collected at the time of admission. 3ml of venous blood was collected in heparinised tube for CRP. C-Reactive Protein was estimated using Latex Agglutination assay. The reagent was a suspension of polystyrene latex particles of uniform size coated with anti human CRP antibodies. Latex particles allow visualisation of the antigen antibody reaction. If C-reactive protein was increased in the serum, the reaction of the antigen with the antibody results in agglutination which is evident in the latex particles. Results are expressed in mg/L of C-reactive protein based on the WHO International Standard for Human C-Reactive Protein.

Statistical Analysis: Data were processed using SPSS software. All values were expressed as mean ± Standard deviation / median. Comparison of absolute eosinophil count between the two groups was done using student 't' test.

RESULTS:

A total of 104 patients who were admitted in Rajiv Gandhi Government General Hospital in the study period (February 2018 to November 2018) with an eventual diagnosis of

perforative peritonitis and meeting the inclusion criteria and the exclusion criteria were chosen for present study. These patients were allocated into two groups based on the outcome as: a mortality group or a survival group. Among them, 88 patients were found to be in the survival group and 16 patients were found to be in the mortality group. The age group of the patients in current study ranged from 24 years to 75 years. In present study a total of 86 patients were male and 18 patients were female. The characteristics of the patients like age,type of perforation,CRP were tabulated.

Table no.1 Characteristics of patients in the survival group

PARAMETER	MEAN ± SD	RANGE	95% CI	MEDIAN
AGE (YEARS)	48.24 ± 12.03	24 – 75	45.69- 50.79	48
M:F	76:12			
CRP (mg/dl)	35.43 ± 15.22	5 – 79	32.21 – 38.66	35

Table 1 showing the characteristics of the patients in the survival group.The age,CRP values were expressed as mean±SD.Their median values and range of distribution are also given.

Table 2 showing the characteristics of the patients in the mortality group.The age, CRP values were expressed as mean±SD. Their median values and range of distribution are also given.

Table 2: Characteristics of patients in the mortality group.

PARAMETER	MEAN ± SD	RANGE	95% CI	MEDIAN
AGE (YEARS)	53.75 ± 8.68	34 – 66	49.12 – 58.38	55
M:F	10:6			
CRP (mg/dl)	89.75 ± 15.70	58 – 110	81.39 -98.11	92

Table 3: Comparison of CRP with the type of perforation.

PERFORATION	N (%)	CRP Mean ± SD	CRP P
Peptic	55 (53%)	45.13 ± 25.92	0.56
Ileal	41 (39%0	42.66 ± 24.76	0.71
Appendicular	5 (5%)	39 ± 25.58	0.66
Colonic	3 (3%)	42.67 ± 8.02	0.94

Table 3 shows the comparison between various types of perforation and their CRP levels. Among them it was found that the peptic (53%) perforations were common est(commonly found in the first part of duodenum and in the prepyloric of the stomach) followed by ileal (39%),appendicular (5%) and colonic (3%) forms of perforation. P value <0.05 was considered statistically significant. It was found that there was no statistically significant increase in CRP levels with respect to the type of perforation.

Table 4: Distribution of CRP among the patients.

PARAMETER		Mean ± SD	T	P
CRP	SURVIVORS	35.43 ± 15.22	13.07	0.0001
	DEAD	89.75 ± 15.70		

Table 4 showing CRP distribution between the two groups.P value <0.05 was considered statistically significant.There was statistically significant difference in CRP levels between the two groups. This shows that increase in CRP levels are associated with adverse outcome in perforative peritonitis patients.

DISCUSSION :

Perforation peritonitis is a frequently encountered surgical emergency in tropical countries like India, most commonly affecting young men in their prime of life. Most of these patients present with perforation of the upper gastrointestinal tract.In a majority of the cases, presentation to the hospital is late with well-established generalized peritonitis with purulent / fecal contamination and varying degrees of septicemia. Assuming that the patients with peptic ulcer perforation are septic upon admission, the determinants of mortality in sepsis should hold true for perforation peritonitis as well. It is necessary to recognize patients at risk preoperatively and prepare for an intensive postoperative management strategy. This becomes more significant in authors' setup, where the intensive care facilities are limited and overwhelmed by the number of patients.

C-Reactive Protein(CRP) is an acute phase protein which is essential for the host defence against inflammation particularly in infection. Acute phase CRP values show no diurnal variation and are not affected by food. Liver cell failure decreases CRP production. No other pathologies or drugs affects acute phase CRP levels unless the disease process affects the pathway of synthesis[4]. C-Reactive Protein(CRP) is one of the most sensitive acute phase reactant in myocardial infarction, stress, trauma, infection, inflammation, surgery and neoplastic proliferation. The increase is more for bacterial than viral infections.C-Reactive Protein(CRP) starts rising within 6 to 12 hours and peak levels are at 48hours. C-REACTIVE PROTEIN is elevated in Acute inflammation (Bacterial infection, Pneumococcal pneumonia, Acute rheumatic fever ,Bacterial endocarditis ,Staphylococcal osteomyelitis) and Tissue injury (Surgery, Acute myocardial ischemia) [5]

Clinical signs of infection are nonspecific, and the identification of the culprit pathogen is not available in the early hours. Sepsis is associated with a strong acute-phase response resulting in pronounced changes in the concentrations of many plasma components. Apart from their values in discriminating no-sepsis-SIRS from sepsis, several biochemical indicators have been assessed regarding their potential in predicting prognosis. Of these procalcitonin appears to be good diagnostic marker of sepsis[6].

However, some authors have questioned its capacity to discriminate infection from controls.These observations only confirm that testing for goodness of fit with the data, to which it is being applied, is a must for any prognostic scoring system or biomarker. Geographical variation in the different patient subsets makes such testing and validation mandatory. Since each surgical/medical unit serves a different patient population, each score system/biomarker must be calibrated and may have different cut-off values (disease or setting specific) in the individual hospital to ensure that the model is applicable for the patient material involved, before it is accepted as quality standard.Clearly, the septic syndrome is far too heterogeneous and complex to be reduced to a single cut off of any surrogate marker.

Many research and educational programs are being done at national and international level to improve the outcome of severe sepsis. On the other hand, the developing countries are struggling in many ways to identify the patients as high risk and to treat them with intensive therapy since the resources are limited. CRP has been found to be a promising marker of sepsis but cost constraints prevent it use as a routine marker of sepsis especially in critical care setup in developing countries[7].

CONCLUSION :

From this study, we conclude that CRP is a reliable marker of survival and it allows timely identification of high-risk patients. It can be used as a marker for risk stratification in perforative peritonitis patients. CRP has the necessary sensitivity and specificity in addition to easy methodology as seen with other markers of sepsis and that there is no correlation between CRP levels and the type of perforation.

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