Evaluation of C Reactive Protein Levels with Reference to Clinical Suspicion of Appendicitis

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Abstract: C reactive protein is an acute phase reactant protein expressed in hepatocytes in response to inflammation, bacterial infection, trauma, necrosis of tissues and malignancy. The aim of this study is establish the correlation of CRP in clinically suspicious appendicitis. The study consisted of 100 patients who underwent appendicectomy for the treatment of appendicitis. Biopsies of all these patients sent to histopathology were examined. The test was found to have a sensitivity of 85.71%, specificity of 78.26% with PPV of 92.95% and NPV of 62.06%. It was concluded that elevated CRP levels can confirm surgical indication of appendicitis confirmed with clinical signs and symptoms and ultrasonography. It can be used as an adjuvant to reduce complication rate and avoid negative laparotomies.

Keywords: C reactive protein, appendicitis, appendicectomy

1. Introduction

The name CRP arose because it was first identified as a substance in the serum of patients with acute inflammation that reacted with the 'c' carbohydrate antibody of the capsule of pneumococcus. CRP is an acute - phase reactant protein that is primarily induced by the IL - 6 action on the gene responsible for the transcription of CRP during the acute phase of an inflammatory/infectious process. CRP is a member of pentaxin family of plasma protein, which are unrelated to other known protein, but which are themselves stably conserved in vertebrate evolution, composed of five identical non - glycosilated 206 amino acid polypeptide subunits, non - covalently associated in a disc with cyclic pentameric symmetry. There is single functional copy of the human gene for CRP, located on chromosome 1 and no polymorphism of either the coding sequence or of the protein itself and yet been described, nor has any individual lacking CRP identified. CRP is expressed only in hepatocytes and its production is regulated by cytokines, particularly IL - 6. In response to bacterial infection, trauma, necrosis of tissues and most forms of inflammation and malignant neoplasia; CRP production is rapidly and dramatically increased and serum levels can exceed 300mg/l by 48 hours after acute event. A recent meta - analysis has shown that there is five - fold increase in the positive likelihood ratio for acute appendicitis when both white blood cells count and C - reactive protein are elevated.

2. Materials and Methods

This study was performed on 100 patients who were operated for treatment of appendicitis. Patients having a complaint of abdominal pain were examined by a surgeon. For establishing a diagnosis, careful patient history was obtained. Physical examination of the patient was done by a surgeon and was repeated as needed. This was followed by Alvarado scoring, which was done for every patient. In all cases, diagnosis was established by detecting right lower quadrant tenderness, guarding and rebound tenderness. Serum CRP concentrations were measured before the operation by CRP kit. In this study, Alvarado scoring, ultrasonography, intra operative findings and biopsy reports were recorded.

3. Results

According to the study, 29 patients were CRP negative. Out of these in intra - op none (0) had perforated appendix, 11 patients had an inflamed appendix and 18 had minimally inflamed appendix. The remaining 71 patient were CRP positive, of which 5 had minimally inflamed appendix, 50 had inflamed appendix and 16 had a perforated appendix.

	CRP	CRP	
	positive	negative	Total
Minimally inflamed appendix	5	18	23
Inflamed appendix	50	11	61
Perforated appendix	16	0	16
Total	71	29	100

	CRP	CRP	
Biopsy report	positive	negative	Total
Subacute appendicitis	5	18	23
Acute appendicitis	11	3	14
Acute ulcerative appendicitis	38	5	43
Acute suppurative appendicitis	6	2	8
Acute necrotizing appendicitis	6	0	6
Acute gangrenous appendicitis	5	1	6
Total	71	29	100

Intraoperative findings and CRP cross tabulation

As per the histopathological results, CRP was positive in only 5 out of 23 patients (21.74%) with subacute appendicitis, 11 out of 14 patients (78.57%) in acute appendicitis, 38 out of 43 patients (88.37%) in acute ulcerative appendicitis, 6 out 8 patients (75%) in acute suppurative appendicitis, in all six patients (100%) of acute necrotizing appendicitis and in 5 out of 6 patients (83.33%) in acute gangrenous appendicitis. Histopathology and CRP cross tabulation

Volume 13 Issue 4, April 2024 Fully Refereed | Open Access | Double Blind Peer Reviewed Journal www.ijsr.net

The following table shows the negative and the positive predictive value of this test.

	Inflamed or perforated appendicitis	Minimally inflamed appendicitis	
CRP positive	66 (a)	5 (b)	71
CRP negative	11 (c)	18 (d)	29
	77	23	100

a= true positive b= false positive c= false negative d= true negative

Sensitivity (a/a+c) = 85.71%

Specificity (d/d+b) = 78.26%

Positive predictive value (a/a+b) = 92.95%

Negative predictive value (d/c+d) = 62.06%

4. Discussion

Acute appendicitis is the most common surgical emergency. Early diagnosis of appendicitis can prevent complications like perforation, abscess formation and sepsis. Preventing these complications not only decrease the morbidity of the patient but also decreases their cost by shortening hospital stay. Despite recent advances, accurate diagnosis of appendicitis is largely clinical, which is based on brief history of abdominal pain, nausea, migration of pain to the right iliac fossa and signs of local peritonitis. The diagnostic accuracy based on such clinical findings is around 70 - 80%. However, in some cases, clinical presentations are atypical and diagnostic errors are likely. C - Reactive protein is an acute phase protein which is used as a screening device for occult inflammation and can be used as a diagnostic tool. The diagnostic value of CRP concentration in predicting appendicitis appears to be reliable and widely applied to the patients with suspected appendicitis as per numerous studies. In this study of 100 patients, maximum number of patients are aged between 20 - 30 years (45%) with preponderance in the male gender (71%). All patients had complaints of pain in abdomen followed by vomiting (38%), fever (26%) and constipation (15%). Tachycardia was observed in 32% patients, fever (temperature > 99°F) in 26% patients, rebound tenderness in 22% and guarding in 14%. Other specific signs were Rovsing's and psoas signs which were observed only in 8%. On clinical assessment of patients and evaluation according to Alvarado scoring, maximum patients (34%) had the score of 5 followed by score of 6 in 20% cases. Intraoperative findings show a strong association of inflammation with CRP levels as 78.2% patients with minimally inflamed appendix (mean 2.4 with standard deviation of 0) had CRP negative values whereas, 82% patients with inflamed appendix (mean 4.8 with standard deviation of 1.71) and 100% patients with perforated appendicitis (mean 9.15 with standard deviation of 1.80) had CRP positive values.29% of patients had non reactive CRP levels. This association is further strengthened by histopathology findings as CRP titers were positive only in 21.7% of subacute appendicitis compared to 78% in acute appendicitis, 88% in acute ulcerative appendicitis, 75% in acute suppurative appendicitis, 83% in acute gangrenous appendicitis and 100% in acute necrotizing appendicitis. This proves, not only is CRP positive titer associated with acute appendicitis but also specificity increases with the severity of appendicitis. In this study, the sensitivity was 85.71% and the specificity was 78.26% which shows that CRP as a specific marker is of limited value when it comes to diagnosing appendicitis especially in its early onset. A high positive predictive value of 92.95% shows that raised CRP titers yield inflammation of appendix on histopathology examination. The negative predictive value of this study is 62.06%.

5. Conclusion

Elevated serum CRP levels serve as an independent marker for the surgical indication of acute appendicitis confirmed with clinical signs and symptoms and other routine modalities. It can be used frequently as a diagnostic tool for appendicitis, so that complication rate can be drastically reduced and negative laparotomies can be avoided. If CRP is within normal limits and the diagnosis is indeterminate, it is advisable to observe these patients with serial clinical examination. CRP is an adjuvant tool in the diagnosis of appendicitis along with clinical examination, CBC and ultrasonography.

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Volume 13 Issue 4, April 2024

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