Research Paper

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Evaluation Of C-Reactive Protein Level And Total Leucocyte Count in Acute Appendicitis

Medical Science

KEYWORDS : Creactive protein, Total leukocyte count, Acute appendicitis

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INTRODUCTION

Acute appendicitis is one of the most common surgical emergency and is usually a clinical diagnosis. Many patients may present with typical history and examination findings. However 30.0% of the cases have atypical clinical presentation and it remains a diagnostic dilemma even for the senior surgeons , even in the presence of multiple diagnostic tool, and this can lead to its complications like appendicular abscess, appendicular perforation, peritonitis.1,2,3

Western literatures report that 6% of population have risk of suffering from appendicitis during their lifetime.4 The overall mortality rate for appendicitis has decreased from about 26% to less than 1% because of antibiotics and early surgical intervention, but in elderly it is approximately 5 to 15%.The morbidity due to appendicular perforation ranges from 17% to 40%. The perforation rate is higher in both elderly and children.5

Diagnosis of acute appendicitis is established by surgeon's clinical impression depending on presenting history, clinical examination and relevant laboratory investigations. A typical presentation is not so common as many inflammatory and non-inflammatory conditions mimic appendicitis. A misdiagnosis might result in negative exploration, while delayed diagnosis results in complications like appendicular perforation and abscess. Therefore surgeons are more inclined to operate, when diagnosis is probable rather than wait until it is certain.

Recently, C Reactive Protein (CRP) is considered as the one of the indictor of acute appendicitis. It is one of the acute phase reactant protein that may rise in concentration during acute phase response to inflammation. It is not disease specific marker but it offers valuable diagnostic information about the presence of acute infection with concomitant evaluation of patient history and physical examination.

Thus, this study is an attempt to evaluate the significance of total leukocyte count and CRP in diagnosing acute appendicitis where no other obvious diagnosis of concern is being considered

OBJECTIVES

- To individually correlate CRP and total leukocyte count with histopathology report in case of acute appendicitis
- To evaluate the efficacy of combining both CRP and TLC in acute appendicitis.
- To interpret how these investigations can be used effectively to improve the diagnosis and management of acute appendicitis.

MATERIALS AND METHODS

SOURCE OF DATA: This study was performed on 114 patients who have been clinically diagnosed to have Acute Appendicitis and who were posted for emergency appendicectomy in General Surgery Department of RL Jalappa Hospital attached to Sri Devaraj Urs Medical College, Tamaka, Kolar during the period from January 2014 to June 2015

METHOD OF COLLECTING DATA:

Sample size: Minimum of 60 study subjects of Acute Appendicitis

Sampling method: Simple random sampling

Inclusion criteria

All patients clinically diagnosed to have acute appendicitis and subjected to appendicectomy.

Exclusion criteria

1) Concomitant conditions where CRP or Leukocyte Count is elevated eg. Rheumatoid arthritis, SLE, glomerular nephritis, gout, inflammatory bowel disease
2) Patient with appendicular mass, abscess or generalised peritonitis.

Clinical diagnosis of acute appendicitis was done in the Department of Surgery, based on symptoms of pain, migration, nausea and vomiting, anorexia, fever and signs of peritoneal inflammation like right iliac fossa tenderness, rebound tenderness and guarding. Once acute appendicitis was suspected, patient was subjected to routine investigations as per the hospital protocol. Urine microscopy was performed in all cases. Elderly patients were subjected to further investigations as part of pre-anaesthetic work up including X-ray chest, ECG etc.

CRP, Total leucocyte count was done in all cases. WBC count of more than 10,000 cells/mm3 was considered as Leukocytosis. Ultrasonography of abdomen was done in most of the cases to confirm diagnosis and rule out other causes of pain abdomen. CRP more than 6 mg/dl was considered to be positive. No special preparation of the patient was required prior to sample collection by approved techniques. When there was delay, the sample was stored at 2-8°C. Maximum period of storage was 72 hours. Patients with strong suspicion of acute appendicitis were advised emergency appendectomy. After obtaining consent, patients were operated and the appendectomy specimen was sent for histopathological examination. The HP report was considered as the final diagnosis.

The patients were meticulously monitored in the post-operative period for any complications. All patients were followed up in the outpatient department for a period of two months.

RESULTS: Apart from the routine investigations all the cases were subjected specifically to the following two investigation i.e. W.B.C. count and CRP, to evaluate their role in accurately diagnosing a case of acute appendicitis. All the cases were subjected for histopathological examination which was considered as gold standard to confirm the diagnosis. The following observations were made in the study.

AGE DISTRIBUTION: The age of the patients ranged from 8-65 years, with a mean age of 23.96 ± 9.56years.

Table 1: Age distribution

Out of 114 cases, most common presenting age group is 21-30 years- 44 cases (38.6%), followed by age group of 10-20 years- 41

cases (36%), and age group of 31-40 years- 21 cases (18.4%). The least number of patients were seen in the age group <10 years- 5cases (4.4%).

Age in years	No. of patients	%
<10	3	2.6
10-20	41	36.0
21-30	44	38.6
31-40	21	18.4
>40	5	4.4
Total	114	100.0

Table2 : Gender distribution

Gender	No. of patients	%
Female	48	42.1
Male	66	57.9
Total	114	100.0

In the present study, out of 114 cases, 48(42.1%) patients were females and the remaining 66 (57.9%) were males. The male to female ratio in the present study is approximately 1.3:1.

Table 3: Distribution of symptoms and signs

Symptoms	No. Of patients (n=114)	%	Signs	No. of patients (n=114)	%
Pain abdomen	114	100.0	RIF Tenderness	114	100.0
Migration of pain to RIF	41	36%	Rebound tenderness	37	32.45
Anorexia	36	31.57	Guarding	10	8.7
Vomiting	65	57.01	Rovsing's sign	25	21.9
Fever	45	39.46	Psoas sign	0	0.0
Others	0	0.0	Temp (>99ºF - FB)	44	38.6
-	-	-	Tachycardia >90	16	14.1

Pain abdomen was the presenting complaint in all the cases in our study. 41 (36%) of them had migration of pain to the right iliac fossa. The next common symptom was vomiting in 65 (57.01%) subjects followed by fever in 45 (39.5%) subjects and anorexia in 36(31.6%) subjects.

Among clinical signs, right iliac fossa tenderness was present in all cases (100%), rebound tenderness was present in 37(32.45%) cases, guarding was present in 10(8.8%) of cases, which reflects severity of inflammation. Other peritoneal signs like Rovsing sign was elicited in 25(21.9%) cases.

Table 4: TLC distribution

TLC	No. of patients	%
<10	47	41.2
>10	67	58.8
Total	114	100.0

Out of 114 cases, 58.8 % of the cases had leukocytosis with more than 10,000 T/cumm.

Table 5: CRP distribution

Out of 114 patients clinically diagnosed to have acute appendicitis, CRP was positive in 74.56% of the cases.

CRP	Total
Negative	15(13.15%)
Positive	85(74.56%)
Total	114(100%)

Table 6: HPR findings in relation to TLC levels

HPR	TLC		Total
	<10	>10	
AA	39(83%)	48(71.6%)	87(76.3%)
CA	5(10.6%)	6(9%)	11(9.6%)
GA	0(0%)	10(14.9%)	10(8.8%)
PA	0(0%)	2(3%)	2(1.8%)
RA	3(6.4%)	1(1.5%)	4(3.5%)
Total	47(100%)	67(100%)	114(100%)

P=0.008**, Significant, Fisher Exact test

Out of 67 subjects who had leukocytosis, 71.6% turned out to be acute appendicitis, 9% of the cases were chronic appendicitis, 14.9% were gangrenous, 3% were perforated and 1.5% were recurrent appendicitis on histopathological examination which is **statistically significant.**

Table 8: CRP findings in relation to HPR findings

CRP	HPR					Total
	AA	CA	GA	PA	RA	
Positive	64(73.56%)	7(63.63%)	9(90%)	2(100%)	3(75%)	85(74.5%)
Negative	23(26.44%)	4(36.36%)	1(10%)	0	1(25%)	29(25.4%)
Total	87(100%)	11(100%)	10(100%)	2(100%)	4(100%)	114(100%)

P=0.656, Not significant, Fisher Exact test

Out of 87 patients of acute appendicitis (confirmed by HPE), only 64 (73.56%) cases were positive for CRP, rest 23 (26.44%) cases patients had normal CRP. Whereas 7(63.63%) cases of chronic appendicitis, 9(90%) cases of gangrenous appendicitis, 2(100%) cases of perforated appendix and 3(75%) of recurrent appendicitis were positive for CRP, which is not statistically significant.

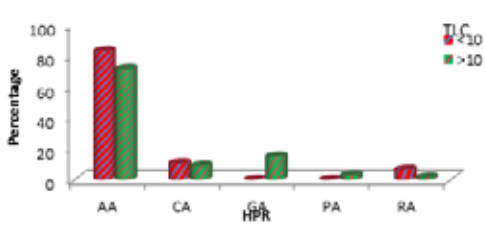
Table 9: CRP in relation to TLC

TLC	CRP(mg/dl)		TOTAL
	NEGATIVE	POSITIVE	
<10	19	22	41
>10	10	63	73
TOTAL	29	85	114

P=0.00, **extremely significant**, Chi-Square test

Among 114 cases clinically diagnosed to have acute appendicitis, both raised TLC and CRP was observed in 63 (55.26%) cases, which was **extremely significant**. Whereas only 19,2% of CRP positive cases did not have leukocytosis and 8.7% of cases with raised TLC were not positive for CRP.

Graph 1: HPR findings in relation to TLC levels



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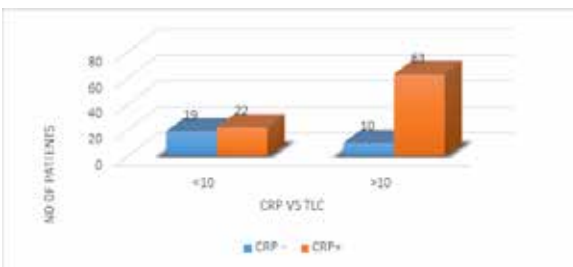
Graph 2: CRP findings in relation to HPR findings

Graph 3: CRP in relation to TLC



DISCUSSION : The present study was done to correlate CRP and TLC with histopathological reports in case of acute appendicitis and to evaluate the efficacy of combined CRP and TLC in diagnosing acute appendicitis.

The study was conducted in Department of General Surgery, R.L.Jalappa Hospital And Research Centre, attached to Sri Devaraj Urs Medical College, Tamaka, Kolar, from period of January 2014 to June 2015 on 114 patients who have been clinically diagnosed of acute appendicitis.

In a study by CS Agrawal et al, age of the patients ranged from 6 years to 60 years. Maximum number of patients i.e 86 (59.2%) were from the age group of 11-30 years.73 Appendicitis is common in the age group of 20 - 29 years and <20 years in this study. Appendicitis reaches its peak incidence in the teens and early 20's.Male predominance is seen in the present study.

In our study, pain abdomen was the presenting complaint in all the patients. The next common symptom was vomiting followed by fever and anorexia. The most common clinical sign was right iliac fossa tenderness which was present in all the cases. In 70% of the cases the clinical presentation is typical and there is no difficulty in making a diagnosis. The remaining 30% have atypical clinical presentation which make the diagnosis difficult.

Many prospective studies have demonstrated that the accuracy of preoperative clinical diagnosis lies in the range of 70-78%. Thus, giving a negative appendicectomy rate around 20.0-25.0% on average.74A negative appendicectomy ranging from 10.0-44.0 has been considered acceptable by various authors. In our study, there were no negative laparotomies as clinical diagnosis was found to be correct in all the cases.

In our study, the total leucocyte count was > 10,000 cells / cumm in 67 (58.8%) patients .Various studies evaluating TLC in diagnosis of acute appendicitis have variable results. 80–85% patients with acute appendicitis will have TLC count of more than 10,000/cmm.75A raised TLC is regarded as sensitive test for diagnosis of acute appendicitis but is not diagnostic because of its lower specificity.76The diagnostic value of TLC is increased when combined with neutrophilia and C-reactive proteins.

C – Reactive protein was found to be positive in 85 (74.56%) patients. In the present study (76.3 %) cases were histopathologicaly found to be acute appendicitis.

Marchand et al concluded in their study that WBC > 10.5 x 109/L was one of the single best test for diagnosis of acute appendicitis with highest sensitivities amongst all the tests examined (81-84%).77

According to study done by JM Goonroos et al WBC was the test of choice in diagnosing uncomplicated acute appendicitis, however it is a poor predictor of protracted inflammation.78 This is supported in study by David and Berchley et al. The WBC count when done individually distinguishes normal appendix from uncomplicated acute appendicitis. But does not distinguish uncomplicated from complicated appendicitis.79 Coleman C et al reported that WBC is a poor predictor of severity of disease.80 Vermenum et al after evaluating 221 patients concluded that WBC count did not significantly influence the surgical decision making.81

Many reports have investigated the value of CRP in improving the diagnostic accuracy of acute appendicitis with conflicting results. A multivariate analysis by Oosterhuis et al82 showed that serial CRP measurement can improve the accuracy of diagnosing acute appendicitis. Other reports did not support this view. In addition, a meta-analysis of 22 published articles concluded that CRP is a test of medium accuracy in diagnosing acute appendicitis.

Leukocytosis (> 10,000 / cumm) was found in in 67 cases of histopathological proven appendicitis cases, out of which 71.6% turned out to be acute appendicitis, which is statistically significant (p=0.008).

In a study by Hyder et al, it was observed that out of 100 cases, 81 cases had histopathological features of acute appendicitis, out of which 62 cases had leukocytosis of > 10,000.83 In another study by Mostafa D et al, it was noticed that 214 cases had acute appendicitis, 102 cases were chronic appendicitis, 36 were gangrenous and 25 were perforated appendicitis.84 In another study by CS Agarwal et al, 81 patients were histologically found to have acute appendicitis with leukocytosis of > 11,000 per cumm.73 In all these studies it was noted that TLC was a significant variable in diagnosing acute appendicitis. Sengupta A et al in their study on 98 patients found that TLC was raised to > 11,000 in 85 cases with significant p value of 0.012.85

Out of 87 patients of acute appendicitis (confirmed by HPE), only 64 (73.56%) cases were positive for CRP, which is not statistically significant.

In a study by CS Agarwal et al, Appendicitis was diagnosed histopathologically in 103 cases. Among these CRP was raised in 77 cases and was normal in 26 cases.73 Davies et al. conducted a study on 60 patients with right iliac fossa pain, CRP and full blood counts were performed and found that 94% of patients had raised CRP with acute appendicitis and 83% of patients had negative CRP results with negative appendictomies.86

Verma et al, measured C-reactive protein in 42 cases admitted to a general hospital with suspected acute appendicitis. Thirty five were operated and thirty one of these with raised CRP had an inflamed appendix. Four cases with normal CRP value had scarred appendix (healed appendicitis) which was confirmed by biopsy reports. These four cases also had normal white blood cell count and ESR.87

Gurleyik et al.compared serum CRP study of 108 patients suspected of having appendicitis on clinical grounds. The diagnosis

depending on surgeon's clinical impression was true in 90 patients and false in 18 patients. This difference was statistically significant (p = 0.0035). They recommend CRP measurement as a routine laboratory test in patients with suspected diagnosis of acute appendicitis.88

Among 114 cases clinically diagnosed to have acute appendicitis, raise in both TLC and CRP was observed in 63 (55.26%) cases, which was extremely significant.

CRP levels were not statistically significant in diagnosing acute appendicitis when considered individually. However, when both CRP levels and TLC were considered, the results were found to be extremely significant with p= 0.00.

Gronroos JM, Gronroos P in a retrospective study studied the preoperative leucocyte counts and C-Reactive protein (CRP) values in three groups of patients operated on for a clinical suspicion of acute appendicitis. They concluded that acute appendicitis is very unlikely when both the leucocyte count and CRP value are normal.78

Asfar S et al.89 conducted a double blind trial in 78 patients to study the impact of a normal (rather than raised) serum C-reactive protein in reducing the rate of negative explorations. White blood count (WBC), CRP and the histopathology findings were correlated. In patients with histopathologically proven acute appendicitis both the WBC count and serum CRP level were significantly raised (p=0.025 and p<0.000 respectively). Serum CRP level was normal in 13 out of 15 negative explorations (normal appendix on histopathology). The specificity and sensitivity of serum CRP was 86.6% and 93.6%, respectively. They concluded that a normal pre-operative serum CRP measurement in patients with suspected acute appendicitis is most likely associated with a normal appendix. Deferring surgery in this group of patients would probably reduce the rate of unnecessary appendicectomies.

Erikson et al. (1994)90 measured serum CRP level and WBC count every four hours in a cohort of 227 patients with suspected acute appendicitis, and reported that it was unusual to find a normal CRP level after 8 hours of observation in the presence of acute appendicitis. If these test results are normal, the surgeon should preferably refrain from operating and consider other differential diagnosis.

All the above studies recommend that CRP and TLC measurement as a routine laboratory test in patients with suspected cases of acute appendicitis as it supports surgeons clinical diagnosis and minimizes negative appendicectomy

CONCLUSION:

Clinical diagnosis was found to be correct in all the cases and hence there were no negative laparotomies for acute appendicitis in our study emphasizing the importance of clinical diagnosis.

Leukocytosis was found to be significant in diagnosing acute appendicitis whereas CRP was insignificant in our study. However, combining CRP and TLC the results were found to be extremely significant.

Thus, it should be stressed that serum CRP estimation does not replace clinical diagnosis, but is useful adjunct in diagnosis of acute appendicitis. Clinical diagnosis is crucial in ruling out alternate diagnosis and other conditions. Thus serum CRP value should be interpreted in combination with clinical findings and leucocyte count.

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