

Predictive Value of TLC and CRP in the Diagnosis of Acute Appendicitis

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Objective: To evaluate the diagnostic accuracy of increased TLC and CRP in making a reliable diagnosis of acute appendicitis by relying on preoperative levels of total leukocyte count and c-reactive proteins.

Subjects and Method: A case control study done in Jinnah Hospital Lahore over one year. Total 150 patients who underwent appendectomy on the basis of clinical suspicion were included. Blood samples including Total Leukocyte count and C Reactive protein were sent preoperatively. Patients were divided in two main categories; **Control**, Group "A" (n 50) with uninfamed appendices and **Cases**, Group "B" (n 68) acute appendicitis and Group "C" (n 32) with complicated acute appendicitis on the basis of operative findings and histopathology. The number of patients with either increased TLC or CRP or both TLC and CRP were sought.

Results: Out of 150 patients there were 85 males and 65 females. In-group A maximum patients 58% turned up having ruptured / hemorrhagic ovarian cysts specificity of CRP was 86% and sensitivity 93% so a CRP levels within normal limits (6 ug/dl) was associated with normal appendices in most of the of times. Very high levels, up to six times normal of CRP were found in complicated acute appendicitis. Positive predictive value of CRP and TLC both (100%) were as good as CRP (100%) alone as compared to TLC, (93%). Negative predictive value of TLC and CRP (66%) was better than TLC (50%) and CRP (50%). So both CRP and TLC are better than either TLC or CRP alone.

Conclusion: CRP should be done as routine laboratory test along with TLC in doubtful cases of acute appendicitis.

Key words: Appendicitis, TLC: total leukocyte count, CRP: C – reactive protein.

Introduction

The diagnosis of acute appendicitis is still difficult and probably the commonest diagnostic problem in clinical surgery.¹ The classical triad of a compatible history, pain at Mc Burneys point and leukocytosis has a diagnostic accuracy of < 80%. Along with these, if ultrasonography, computerized topography or radionuclide scanning are included, it hardly reaches 90%.²

The policy of early operations has been common for many years but may lead to a large number of normal appendices being removed.³ Some people advocated that the policy of "open and see" is better than "wait and see" as an unnecessary operation is better than an unnecessary perforation.⁴ Appendectomy itself can have complications (10-15%) like wound infection, DVT, chest infection, intestinal obstruction etc.⁵

Raised levels of Total leukocyte count (TLC) with clinical signs and symptoms point towards acute appendicitis but patients with perforated appendix can have normal TLC and differential leukocyte count.⁶

C reactive protein is the prototype acute phase reactant, synthesized by liver, its concentration rises within 8 hours of onset of tissue injury/inflammation, peaks 24 – 48 hours and remains elevated as long as continuing tissue inflammation or destruction.⁷ Regular measurement of TLC and CRP in suspected appendicitis may improve accuracy of diagnosing acute appendicitis.⁸

In our setup the role of C-reactive protein and TLC with special reference to acute appendicitis has not been studied

in detail. The purpose of this study is to find out the sensitivity, specificity and diagnostic accuracy of C-reactive protein and TLC for the diagnosis of acute appendicitis.

Material and Methods

It was a retrospective Case-Control study done on 150 patients (85 males and 65 females) in Jinnah Hospital Lahore, Pakistan over one year from July 2002-03. By convenient sampling patients aged 6-65 years, with clinical suspicion of acute appendicitis and they underwent appendectomy, were included in the study. Routine lab tests along with TLC and CRP were sent preoperatively and results were correlated with operative findings and Histopathology where available.

A sample size of 150 with 2: 1 ratio of cases (100) and controls (50) obtained.

Controls, Group "A" were patients who underwent appendectomy on the basis of clinical suspicion and an uninfamed appendix found operatively and histopathologically (subject to availability).

Cases; were patients who underwent appendectomy on the basis of clinical suspicion and confirmed appendicitis on the basis of operative findings and histopathology (subject to availability); Group "B" with uncomplicated acute appendicitis and Group "C" with complicated acute appendicitis.

Pregnancy, Extreme of ages, preexisting disease, immunocompromised status and patients suffering from other acute inflammatory conditions were excluded from the study.

Normal values for TLC; males: $10 \times 10^9/l$, Females:

$9 \times 10^9/l$ and C-reactive protein: $6 \mu g/dl$.

Results were analyzed using SPSS (version 10). Frequency and distribution of different parameters along with predictive values for TLC, CRP and both were calculated.

Results

Mean leukocyte count was significantly lower in patients with uninflamed appendix (group A) than there in complicated appendicitis (group C) and in uncomplicated acute appendicitis (group B). {Group A – C – B}(Table 1).

Mean CRP levels were significantly higher ($p < 0.001$), up to 6 times normal, in patients with complicated acute appendicitis (group C) than in there with uncomplicated acute appendicitis (group B) and there with uninflamed appendix group A. {Group C – B – A}(Table 2).

In group A (Controls): Majority were females 38/50 and 22/38 (58%) having some gynecological problem like twisted, ruptured or hemorrhagic ovarian cyst. Mostly males were in younger age group and mesenteric lymphadenitis was in 6/12 patients. 92% (46/50) patients were having both TLC and CRP within normal limits and in only 8% only TLC was raised (Table 3). So women of child bearing age, with normal TLC and CRP, should be thoroughly assessed by ultrasound and laparoscopy and conservative treatment can be done.

There was no patient with raised CRP so a False positive rate of 0% (0/50).

Table 1: Level of TLC found in different patient groups.

TLC/L	Group A (n = 50)			Group B (n = 68)			Group C (n = 32)		
	T	M	F	T	M	F	T	M	F
5000 – 6000	16	6	10	4	2	2	4	2	2
6000 – 7000	15	3	12	4	2	2	2	2	-
7000 – 8000	12	3	9	7	1	6	-	-	-
8000 – 9000	07	0	3	9	6	3	4	4	-
9000 – 10,000	-	-	-	4	3	1	4	4	-
> 10,000	-	-	-	40	31	9	181	16	2
Total	50	12	28	68	45	23	32	28	4

T: total M: males F: Female

Table 2: Level of C-Reactive Proteins in different patient groups.

CRP $\mu g/dl$	Group A (n = 50)			Group B (n = 68)			Group C (n = 32)		
	T	M	F	T	M	F	T	M	F
Up to 6	50	12	38	48	30	18	2	2	-
7 – 12				6	4	2	8	6	2
13 – 18							6	6	-
19 – 24				9	6	3	8	8	-
25 – 36				5	5	-	8	6	2
Total	50	12	38	68	45	23	32	28	4

T: Total M: Males F: Females Normal value of CRP: $6 \mu g/dl$

Table 3: Comparative levels of TLC & CRP in different groups.

TLC and CRP	Group A (n = 50)			Group B (n = 68)			Group C (n = 32)		
	T	M	F	T	M	F	T	M	F
Both Normal	46 (92%)			12	34	21 (31%)	11	10	2 (6%) 2
Only TLC raised	4 (8%)	-		4	27 (40%)		19	8	-
Only CRP raised	-	-	-	6 (9%)	3	3	16 (50%)	14	2
Both raised	-	-	-	14 (20%)	12	2	14 (44%)	12	2

T: total M: Male F: Female Raised TLC: $M > 10 \times 10^9/l$, $F > 9 \times 10^9/l$ & CRP $> 6 \mu g/dl$.

In group B (Cases) Acute uncomplicated appendicitis: There were 68 patients, 45 males, 23 females. Maximum patients, 40% were having only raised TLC. Where as there was no patient in group C (complicated appendix) with raised TLC (table 1), 2nd to it were raised levels of TLC and CRP 31% (fig. 1). So it appeared that TLC was a better lab test than CRP in diagnosing uncomplicated acute appen-

dicitis.

In group C (complicated acute appendicitis): There were 32 patients mostly males 28 (88%) than females 4 (12%). In this group, Maximum patients 50% were having only raised CRP and second to it were raised levels of both TLC and CRP 44% (table 3). Very high levels of CRP --- (up to 6 times normal) were found and it indicated that CRP

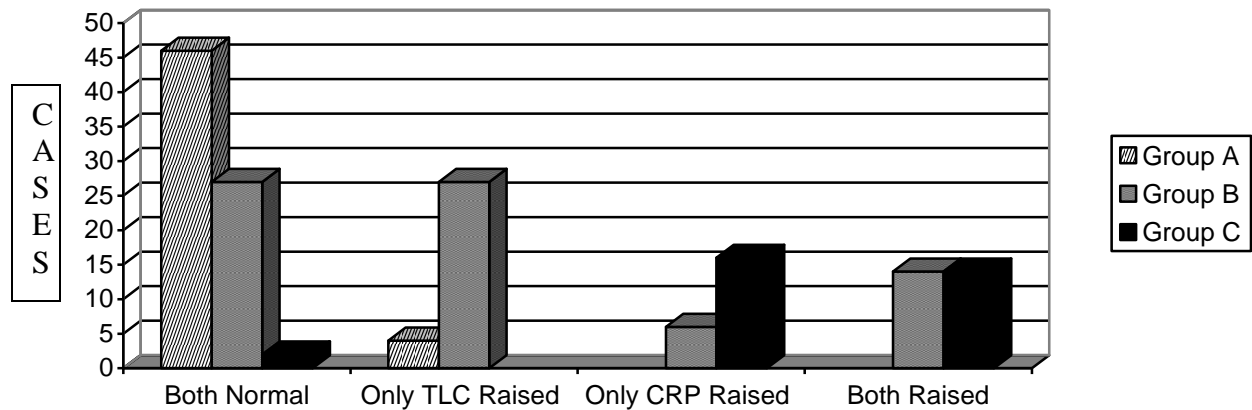


Fig. 1: Comparative levels of TLC & CRP in different groups.

is a better lab test than TLC in the diagnosis of complicated acute appendicitis. High levels of CRP either alone or with raised TLC supported mandatory explorations.

There were 50 patients (20 in group B and 30 in group C) with raised levels of CRP, so a false negative rate of 50% (50/100).

Table 4: Predictive Factors for TLC, CRP and TLC and CRP Both.

TLC	CRP	CRP+	TLC
Sensitivity	55%	50%	55%
Specificity	92%	100%	100%
Positive predictive value	93%	100%	100%
Negative predictive value	50%	50%	66%
Accuracy	67%	66%	77%

Discussion

Avoidance of negative appendectomies and at the same time deciding for mandatory explorations remains the final goal. In this context, the reliability and clinical usefulness of these inexpensive blood tests TLC & CRP is sorted out.

In case of raised TLC; Its Sensitivity of 55%, Specificity of 92% and Accuracy 67% of detecting acute appendicitis was in contrast with a study by Nasir et al⁹ with Sensitivity 74.4%, specificity 72% and accuracy of 74%. This improved accuracy could be because of small sample size (n: 50) and abnormal TLC taken as > 10,000/dl in both sexes. A raised TLC may be highly sensitive for acute appendicitis but its low specificity has decreased its diagnostic value.¹⁰ Increased leukocyte count is usually the earliest laboratory test to indicate appendice inflammation, only during protracted inflammation CRP increase. The leukocyte count does not, however, increase any more in appendice perforation or abscess formation, as reported earlier¹¹ and confirmed in the present study.

In case of raised CRP (>6 ug/dl): Sensitivity of 50%, Specificity of 100% and an accuracy of 66%.of finding acute appendicitis was in contrast to a previous study¹² in which CRP had a very good Sensitivity of 93.5%, Specificity of 80% and an accuracy of 91%.Asfar et al found almost same sensitivity of 93.3% and specificity of 86.6% and pointed that normal CRP is mostly associated with normal appendices, deferring surgery would probably reduce unnecessary appendectomies.¹³

In case of both CRP & TLC: Raised levels showed a sensitivity of 55%, specificity of 100% and an accuracy of 77% in diagnosing acute appendicitis. Increased CRP appears to have better sensitivity but TLC has better specificity, combining these two measurements may bring sensitivity to 100% but specificity declines to 50%.Therefore a negative CRP and TLC may be more informative than a positive response.¹⁴

In all patients with acute appendicitis {Group B&C} (n = 100) either TLC or CRP or both were above normal limits. In a previous study if there was clinical suspicion of acute appendicitis, normal TLC and CRP levels excluded acute appendicitis with a predictive value of 100%.¹ In a study done in children with acute appendicitis, TLC and CRP Both revealed a predictive value of 93%.¹⁵ But in our study 23% (23/100) patients with both values normal turned up as acute appendicitis per-operatively, so accuracy declined to 77%. But this could be explained by the fact that our main criteria was per-operative findings (which is operator dependent) and histological examination when available. (Histopathology was unavailable in 38% cases).Birchley concluded that White cell count, neutrophil count and CRP are most effective in supporting a clinical diagnosis of acute appendicitis in patients with typical features than in excluding the diagnosis.¹⁶

We conclude that sensitivity, specificity, positive predictive value and negative predictive value of CRP and TLC are better than either TLC or CRP alone. We can rely on normal TLC and CRP to exclude acute appendicitis but even

then clinical judgment by an experienced surgeon should be regarded. Very high levels of CRP either alone or coupled with raised TLC warrants mandatory explorations. We recommend that CRP should be done as routine laboratory test along with TLC in the doubtful diagnosis of acute appendicitis.

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