ORIGINAL ARTICLE

C-REACTIVE PROTEIN: AN AID FOR DIAGNOSIS OF ACUTE APPENDICITIS

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Background: Delayed or wrong diagnosis of acute appendicitis in patients results in complications like perforation, gangrene, etc. which carries a significant amount of morbidity and mortality to the patients. Thus, timely diagnosis of acute appendicitis is crucial to prevent these complications. Recently, it was found that serum C-reactive protein (CRP) individually can be a useful marker, thus in resource limited settings (i.e., access to ultrasonography) simple laboratory investigation can be of extreme utility for the diagnosis of acute appendicitis. Current study aimed to ascertain and determine the role of C Reactive Protein (CRP) as a complementary test to decrease the rate of negative appendectomies in tertiary care hospitals of Pakistan. **Methods:** Using non-probability consecutive sampling, 112 patients with the initial diagnosis of acute appendicitis on history and clinical examination were enrolled. A blood sample was taken for serum level of CRP. **Results:** Mean age was 20.8±8.6 years and 51 (45.5 %) patients were males. Pathologic review revealed 100 cases (89.3%) of acute appendicitis, 4 patients (3.6%) had perforated appendix while 8 patients (7.1%) had normal appendix. Sensitivity, specificity, positive and negative predictive value and diagnostic accuracy of C reactive protein >24 mg/lit taking histology as gold standard came out 25.9%, 100%, 100%, 9.4% and 31.25% respectively. **Conclusion:** It was concluded that CRP >48 mg/lit is an indication of perforated appendix and when the surgeon is in fix whether to go conservatively or apply some intervention, CRP can be a good diagnostic aid

Keywords: Acute appendicitis; C Reactive Protein; Diagnostic accuracy; Perforated appendix

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INTRODUCTION

Once a term of fear in far flung areas of subcontinent, still the most common surgical abdominal emergency all over the world is acute appendicitis.[1–6] Mortality associated with appendicitis is not worth mentioning as the procedure is common and well trained surgeons exist and the effected population is young without any comorbidity.[7] History, clinical examination, laboratory and radiological parameters are essential but we are unable to define a single diagnostic test.[2,3,8–10] Diagnosis of acute appendicitis requires subjective approach for diagnosis despite all advancement in imaging and laboratory technologies with resultant either perforated appendices in case of conservative approach or negative surgeries if a proactive attitude is maintained by a surgeon.[11–13] Rate of negative laparotomies is still high depending on different setting ranging from 20–40%.[1,8,13–15]

This trade-off between proactive and conservative approach can be balanced using complementary laboratory investigations which are affordable and available in less developed regions too. In this background, C reactive protein (CRP) has been proposed as a good indicator of acute appendicitis. But level of this acute phase reactant may rise in many conditions. Current study aims to ascertain and determine the role of CRP as a complementary test to decrease the rate of negative appendectomies in tertiary care hospitals of Pakistan as the available evidences show variability in concluded results.

MATERIAL AND METHODS

This cross-sectional study was conducted at Bolan Medical Complex Hospital, Quetta from 03/01/2015 till 28/07/2015. Using non-probability consecutive sampling, 112 patients with the initial diagnosis of acute appendicitis who were admitted in emergency surgery department of Bolan Medical Complex were enrolled after taking informed consent. Diagnosis of acute appendicitis was provisionally made by history and clinical examination by consultant surgeons. Patients' history, physical examination and raised white blood cell count (Leucocytosis) were used by the surgeons whether to admit or discharge the patients suspicious for acute appendicitis.

All patients who were operated on with the initial diagnosis of acute appendicitis included in the study and other patients who were candidate for conservative management based on the surgeon's decision and those with any active infectious or inflammatory diseases were excluded. A blood sample was taken from all patients in the first hours of admission under aseptic condition by a registered nurse and sent to the laboratory within one hour. CRP concentration was measured by immune-turbidometry by an experienced laboratory

technologist. The appendix specimens were sent to Histology department of Allama Iqbal Medical College, Lahore for confirmation of status of removed appendix. Specimens were sent in a sterile container with formalin as preservative.

Data was collected on structured proforma containing background information like age of patients in year, gender of the participant, CRP level and histology report. Data was analysed using SPSS-21. Mean and standard deviation were calculated for age and CRP level and frequency in case of gender and status of appendix on histology. Data was cross tabulated for different ranges of CRP and appendicitis and level of significance was calculated using chi square test of homogeneity or Fisher exact test (if count in each cell is less than 5). Mean distribution of CRP in patients with and without histological diagnosis of Acute Appendicitis was analyzed using independent sample *t*-test. A *p*-value ≤0.05 was considered significant.

RESULTS

The mean age of the patients was 20.8±8.6 years (range 9–60 years). There were 51 males (45.5%) and 61 females (54.5%). Pathologic review of the specimen revealed 100 cases (89.3%) of acute appendicitis, 4 patients (3.6%) had perforated appendix while 8 patients (7.1%) had normal appendix (Table-1). When data was cross tabulated for categories of CRP and appendicitis a significant difference (*p*-value=0.033) resulted showing all patient with perforated appendix have CRP more than 48 mg/litter while all patients with normal appendices had normal CRP (below 6 mg/lit) (Table-2). The mean value of CRP in normal appendix group was 1.5 mg/lit compared to 19.9 mg/lit (difference 95% CI: -23.89 to -12.94) in patients with pathologically confirmed appendicitis (*p*<0.001) (Table-3). Sensitivity, specificity, positive and negative predictive value and diagnostic accuracy of C reactive protein >24 mg/lit came out 25.9%, 100%, 100%, 9.4% and 31.25% respectively. (Table-4)

Table-1: Frequency distribution of CRP and appendicitis (n=112)

	Characteristic	Frequency	Percent
Histology of Appendix	Normal	8	7.1
	Acute Appendicitis	100	89.3
	Perforated Appendix	4	3.6
CRP Categories	Normal (< 6)	65	58.0
	7–12	9	8.0
	13–24	1	.9
	25–48	10	8.9
	>48	27	24.1

Table-2: Cross tabulation between appendix on histology and CRP Categories

		CRP Categories				
		Normal (< 6)	**7–12**	**13–24**	**25–48**	**>48**
Appendix on Histology	**Perforated Appendix**	0	0	0	0	4
	Acute Appendicitis	57	9	1	10	23
	Normal	8	0	0	0	0
Total		65	9	1	10	27

Using Fisher's Exact Test, *p*-value=0.033 (Significant)

Table-3: Distribution of mean C reactive protein level among patients with and without acute appendicitis

	Status of Appendix	n	Mean	SD	SD. Error Mean
C Reactive Protein	**Normal**	8	1.50	.535	.189
	Acute Appendicitis	100	19.91	27.494	2.749

Equal variances not assumed, using independent sample *t* test, *p*-value <0.001

Table-4: 2×2 table showing diagnostic validity of CRP >24 for appendicitis

CRP > 24	Appendicitis		
	Yes	No	
Yes	27	0	27
No	77	8	85
	104	8	112

DISCUSSION

Diagnosis of acute appendicitis is still challenging even after the advent of CT scan, Ultrasonography and diagnostic laparoscopy.[1,8,13,16,17] Current study was undertaken to reduce this dilemma. If CRP comes out to be a valid predictor, we may be able to reduce the rate of negative appendectomies in our poor population.

Mean age in our sampled population came about 21 years which is in accordance data reported by other studies. Male to female ratio was almost

equal with an increasing trend towards female. It may be because of long differential list in female patients presenting with pain in right iliac fossa. The case positivity rate is comparable with previous studies. 89.3% patients had acute appendicitis, 3.6% had perforated while 7.1% have normal appendices on the histological examination. The negative appendectomy rate is in accordance with the international standards which range from 5–15 percent.[1,8,12,13]

There has always been a clinical discussion on the diagnosis of appendicitis. The surgeon has always to suffer uncertainty either to be conservative or go for surgery when he comes across a difficult patient. Most of the signs and symptoms are not sensitive and specific. So, we have to get aid from laboratory examination like total leucocytes' counts and difference measures like therapy. In our population, it was shown that if CRP is more than 48 mg/lit then there is increased risk that we will come across a perforated appendix.

The results of the present study highlighted that CRP though not sensitive (25.9%) but it is quite specific (100%) with high positive predictive value (100%) and low negative predictive value (9.4%) and over all diagnostic accuracy (31.25%) are quite low. A study from Pakistan has reported sensitivity, specificity and positive predictive value of C reactive protein as 85.7%, 75% and 94.5% respectively when cut-off of 48 mg/dl was used.[18] A study conducted in study in general surgical unit of King Fahd Armed Forces Hospital, Jeddah, Saudi Arabia reported CRP showed 78.16% sensitivity and 61.53% specificity.[19] A recent study reported that sensitivity and specificity of CRP to identify complicated appendicitis were 71.0% and 100% respectively at this cut-off of 40.1 mg/dL.

Thus, high CRP levels could possibly predict the diagnosis of complicated appendicitis and facilitate more appropriate surgical care.[20] Sensitivity of 53–88% and specificity of 46–82% was noted in a meta-analysis by Chung JL *et al*.[2] However, a study that uses a lower cut-off of 14 mg/L, reported sensitivity and specificity of 59% and 68% respectively.[10] The positive and negative predictive values were 89% (95% CI: 80–97%) and 27% (95% CI: 14–39%), respectively.[10] It has been reported that the sensitivity, specificity, and positive predictive values of the C-reactive protein (CRP), white blood count (WBC) and Neutrophils percentage (NP), tests in combination were 95.3%, 72.2%, and 95.3%, respectively thus a combination of these three tests significantly increases the accuracy.[21]

CONCLUSION

It is concluded that C Reactive Protein greater than 48 mg/lit is an indication of perforated appendix and when the surgeon is in fix whether to go conservatively or apply some intervention; CRP can be a good diagnostic aid. Further studies with time series analysis are needed covering all other confounding factors

AUTHORS' CONTRIBUTION

MAB: Conception and design of the article and critical revision. KMB and JA: Data analysis and drafting the manuscript.

REFERENCES

1. Crownover BK, Bepko JL. Appropriate and safe use of diagnostic imaging. Am Fam Physician 2013;87(7):494–501.
2. Yu CW, Juan LI, Wu MH, Shen CJ, Wu JY, Lee CC. Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. Br J Surg 2013;100(3):322–9.
3. Kaya B, Sana B, Eris C, Karabulut K, Bat O, Kutanis R. The diagnostic value of D-dimer, procalcitonin and CRP in acute appendicitis. Int J Med Sci 2012;9(10):909–15.
4. Ng KC, Lai SW. Clinical analysis of the related factors in acute appendicitis. Yale J Biol Med 2002;75(1):41–5.
5. Bachoo P, Mahomed AA, Ninan GK, Youngson GG. Acute appendicitis: the continuing role for active observation. Pediatr Surg Int 2001;17(2-3):125–8.
6. Tehrani HY, Petros JG, Kumar RR, Chu Q. Markers of severe appendicitis. Am Surg 1999;65(5):453–5.
7. McGowan DR, Sims HM, Zia K, Uheba M, Shaikh IA. The value of biochemical markers in predicting a perforation in acute appendicitis. ANZ J Surg 2013;83(1-2):79–83.
8. Thirumallai S, Wijesuriya SR, Mitchell A, Delriviere L. Predictive value of C-reactive protein with Alvarado score in acute appendicitis. ANZ J Surg 2014;84(5):335–6.
9. Shogilev DJ, Duus N, Odom SR, Shapiro NI. Diagnosing appendicitis: evidence-based review of the diagnostic approach in 2014. West J Emerg Med 2014;15(7):859–71.
10. Jangjoo A, Varasteh AR, Bahar MM, Meibodi NT, Aliakbarian M, Hoseininejad M, *et al*. Is C-reactive protein helpful for early diagnosis of acute appendicitis? Acta Chir Belg 2011;111(4):219–22.
11. Leeuwenburgh MM, Stockmann HB, Bouma WH, Houdijk AP, Verhagen MF, Vrouenraets B, *et al*. A simple clinical decision rule to rule out appendicitis in patients with nondiagnostic ultrasound results. Acad Emerg Med 2014;21(5):488–96.
12. Panagiotopoulou IG, Parashar D, Lin R, Antonowicz S, Wells AD, Bajwa FM, *et al*. The diagnostic value of white cell count, C-reactive protein and bilirubin in acute appendicitis and its complications. Ann R Coll Surg Engl 2013;95(3):215–21.
13. Yetkin G, Basak M, Işgör A, Kebudi A, Akgun I. Can negative appendectomy rate be decreased by using spiral computed tomography without contrast material? Acta Chir Belg 2002;102(5):334–7.
14. Atema JJ, Gans SL, Beenen LF, Toorenvliet BR, Laurell H, Stoker J, *et al*. Accuracy of White Blood Cell Count and C-reactive Protein Levels Related to Duration of Symptoms in Patients Suspected of Acute Appendicitis. Acad Emerg Med 2015;22(9):1015–24.
15. Abbas MH, Choudhry MN, Hamza N, Ali B, Amin AA, Ammori BJ. Admission levels of serum amyloid a and

procalcitonin are more predictive of the diagnosis of acute appendicitis compared with C-reactive protein. Surg Laparosc Endosc Percutan Tech 2014;24(6):488–94.
16. Teo AT, Lefter LP, Zarrouk AJ, Merrett ND. Institutional review of patients presenting with suspected appendicitis. ANZ J Surg 2015;85(6):420–4.
17. Al-Abed YA, Alobaid N, Myint F. Diagnostic markers in acute appendicitis. Am J Surg 2015;209(6):1043–7.
18. Aslam V, Hussain S, Khan MS, Khan SM, Ullah R. C-reactive protein and total leukocyte count in the diagnosis of acute appendicitis. Med Forum 2015;26(6):2–5.
19. Muzaffar N, Bhatti S. Diagnostic value of total leucocyte count and C-reactive protein in acute appendicitis. Pak J Med Health Sci 2014;8(3):508–9.
20. Lai CY, Leung YK, Graham CA. Could C-reactive protein be a potential biomarker of complicated acute appendicitis? Hong Kong J Emerg Med 2014;21(6):354–60.
21. Xharra S, Gashi-Luci L, Xharra K, Veselaj F, Bicaj B, Sada F, *et al*. Correlation of serum C-reactive protein, white blood count and neutrophil percentage with histopathology findings in acute appendicitis. World J Emerg Surg 2012;7(1):27.

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