

Accuracy of C-Reactive Protein and Procalcitonin in Differentiating between Complicated and Non-complicated Acute Appendicitis Patients in Babylon Province

Raad Gazy Al Sehlany, Moad E. Al-Gazally, Mohend A. N. Alshalah

Department of Chemistry and Biochemistry, College of Medicine, University of Babylon, Hilla, Iraq

Abstract

Background: Clinical care may be influenced by the ability to predict whether a patient has complicated appendicitis at the time of presentation. However, it is unclear whether prehospital or in-hospital factors are associated with complicated appendicitis. We also want to know if C-reactive protein (CRP) and procalcitonin (PCT) can be used as supporting factors for Alvarado Score associated with complex appendicitis. **Objectives:** The aim of this study is to know the possibility of adding CRP and PCT to support the diagnostic protocol for differentiating between complicated acute appendicitis and noncomplicated acute appendicitis by knowing the sensitivity and specificity of each of them, as well as knowing which is more acceptable to add to the diagnostic protocol. **Materials and Methods:** A cross-sectional study was carried out in the Emergency Unit at AL-Hilla Teaching Hospital in Babylon province, Hilla city, between October 2021 and January 2022. There were a total of 90 patients; CRP and PCT were measured for patients by enzyme-linked immunosorbent assay method, in addition to knowing their Alvarado score. SPSS software was used to conduct the statistical analysis. **Results:** At the time of surgery, 34 (40%) of the 90 patients had complicated appendicitis, whereas 54 (60%) without complication. The age and gender of the groups did not show any significant difference. The Alvarado score, CRP, and PCT levels all showed a significant difference ($P < 0.05$). The correlation between Alvarado score and biochemical parameters (CRP and PCT) show a significant positive correlation. **Conclusions:** CRP and PCT support Alvarado score to differentiate between complicated acute appendicitis and noncomplicated acute appendicitis, and this is evident from the significantly higher concentrations of both in patients with complicated acute appendicitis than in patients with noncomplicated acute appendicitis.

Keywords: Appendicitis, CRP, Iraq, PCT

INTRODUCTION

The vermiform appendix has been acknowledged as an organ since the late 15th century. It was first described in depth in Leonardo da Vinci's Anatomical Drawings in 1492.^[1] The function of vermiform appendix is immunological. Its function is similar to tonsil, which provides protection to upper GI tract. The appendix acts as a guard for small intestine from different microbes that are present in the large intestine.^[2] Its endocrine cells produce hormones and amines to help with a variety of biological regulations, whereas the lymphoid tissue is important in B-lymphocyte maturation and IgA antibody production.^[3] The common cause of an acute abdomen

requiring surgery is acute appendicitis (AA).^[4] However, the symptoms of AA are similar to those of a variety of other disorders, making early detection difficult.^[5] Appendectomy surgery has been the standard urgent or emergent operation of choice for decades to avoid the development of inflammation that leads to perforation.^[6]

Address for correspondence: Mr. Raad Gazy Al Sehlany,
Department of Chemistry and Biochemistry, College of Medicine,
University of Babylon, Hilla, Iraq.
E-mail: rdaishlany93@gmail.com

Submission: 03-Oct-2022 **Accepted:** 17-Oct-2022 **Published:** 09-Jan-2023

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How to cite this article: Al Sehlany RG, Al-Gazally ME, Alshalah MA. Accuracy of C-reactive protein and procalcitonin in differentiating between complicated and non-complicated acute appendicitis patients in Babylon province. Med J Babylon 2022;19:709-13.

Access this article online

Quick Response Code:



Website:
www.medjbabylon.org

DOI:
10.4103/MJBL.MJBL_230_22

The pathophysiology of noncomplicated and complicated AA is different, and conservative treatment may be recommended for the former.^[7] The majority of AA diagnoses is determined based on the clinical features, with radiography (ultrasonography and computed tomography) investigations saved for a select few.^[8] The Alvarado score is a clinical performance indicator for appendicitis diagnosis. In 1986, the score designed a 10-point clinical scoring system known as MANTRELS for the diagnosis of AA in patients with suspected AA based on symptoms, signs, and medical tests.^[9] In AA, C-reactive protein (CRP) was found to be more useful than bilirubin in detecting perforation.^[10] Unlike CRP, procalcitonin (PCT) is unaffected by sterile inflammation or viral infection. This marks it out as a significant biochemical marker with a wide range of therapeutic applications, including in AA.^[11]

MATERIALS AND METHODS

This study was performed in a cross-sectional methodology. In this study, individuals from the AL-Hilla Teaching Hospital in Hilla city, Babylon province, were used. All samples were taken between October 2021 and January 2022. There were two groups of patients in this study, as shown in Figure 1.

Inclusion criteria

Inclusion criteria were as follows:

1. Informed consent from the patient
2. Histologically confirmed AA.

Exclusion criteria

Exclusion criteria were as follows:

1. Patients treated with anti-inflammatory drugs (e.g., steroid)
2. Patients with a known chronic inflammatory disease
3. Patients with a known acute inflammatory disease
4. Patients with normal appendix
5. Pregnant women
6. Patients with liver disease
7. Patients with thyroid disease.

Determination of human C-reactive protein concentration (Cat. no. E1798Hu)

This kit is an enzyme-linked immunosorbent assay (ELISA). The plate has been precoated with human CRP antibody. CRP present in the samples was added and binds to antibodies coated on the wells. And then biotinylated human CRP antibody was added and binds to CRP in the sample. Then streptavidin-HRP was added and binds to the biotinylated CRP antibody. After the incubation, unbound streptavidin-HRP was washed away during a washing step. Substrate solution was added and color develops in proportion to the amount of human CRP. The reaction is terminated by an addition of acidic stop solution, and absorbance is measured at 450 nm.^[12]

Determination of human procalcitonin concentration (Cat. no. E0977Hu)

This kit is an ELISA. The plate has been precoated with human PCT antibody. PCT present in the samples was

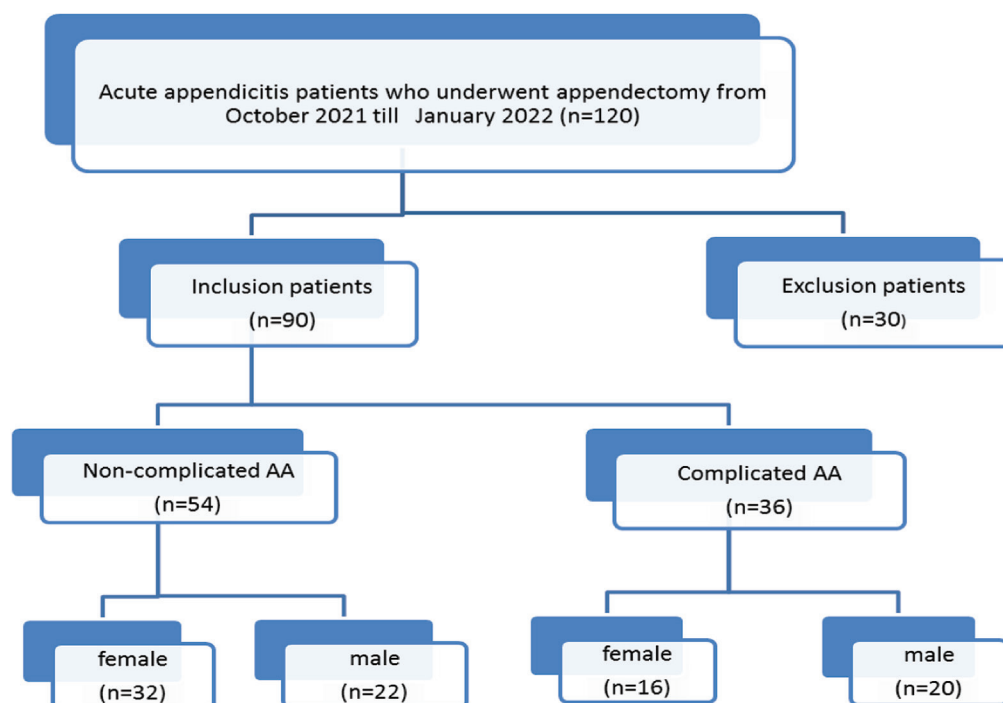


Figure 1: Distribution of number of patients in this study

added and binds to antibodies coated on the wells. And then biotinylated human PCT antibody was added and binds to PCT in the sample. Then streptavidin-HRP was added and binds to the biotinylated PCT antibody. After the incubation, unbound streptavidin-HRP was washed away during a washing step. Substrate solution was added, and color develops in proportion to the amount of human PCT. The reaction is terminated by an addition of acidic stop solution, and absorbance is measured at 450 nm.^[13]

Data analysis

The statistical analysis was done with SPSS software 21. Frequencies and percentages were used to describe categorical variables. To represent continuous variables, means and SD were utilized. To compare the means of two groups, a student t-test was applied. The Pearson chi-square and Fisher exact tests were used to determine the relationship between categorical variables. Pearson correlation coefficient was used to assess the relationship between two continuous variables. A *P* value of less than 0.05 was regarded significant. Nonsignificance was defined as a *P* value greater than 0.05.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form

were reviewed and approved by a local ethics committee according to the document number 1013 in 2/10/2021 to get this approval.

RESULTS

Demographic features of the study groups

Table 1 summarizes the demographics of both complicated and noncomplicated AA patients.

Alvarado score in complicated and noncomplicated acute appendicitis

The mean $\pm$ SD Alvarado score degree of complicated and noncomplicated AA patient groups was shown in Table 2.

Comparison of C-reactive protein values between complicated and noncomplicated acute appendicitis

The mean $\pm$ SD for CRP value of complicated and noncomplicated AA patient groups was shown in Table 3.

Comparison of procalcitonin values between complicated and noncomplicated AA

The mean $\pm$ SD for PCT value of complicated and noncomplicated AA patient groups was shown in Table 4.

Correlation between Alvarado score and biochemical parameters (C-reactive protein and procalcitonin)

As shown in Figures 2, 3, and Table 5, there is a statistically significant positive correlation between the

Table 1: Characteristics of the study group's demographics

Characteristic	Subgroup	Noncomplicated AA group (n = 54)	Complicated AA group (n = 36)	Total patients (N = 90)	P value*
Age (years)	15–35	48 (88.9%)	28 (77.8%)	76 (84.4%)	0.215
	36–55	6 (11.1%)	8 (22.2%)	14 (15.6%)	
Gender	Male	22 (40.7%)	20 (55.6%)	42 (46.7%)	0.173
	Female	32 (59.3%)	16 (44.4%)	48 (53.3%)	
Residence	Urban	21 (38.9%)	13 (36.1%)	34 (37.8%)	0.306
	Rural	33 (61.1%)	23 (63.9%)	56 (62.2%)	

*Nonsignificant values of noncomplicated AA patients versus complicated AA patients, *P* > 0.05

Table 2: Descriptive statistic of Alvarado score between complicated and noncomplicated AA

Patient groups	Number of patients	Mean $\pm$ SD	P value	95% CI
Complicated AA	36	8.31 $\pm$ 0.710	<0.001*S	0.767–1.473
Noncomplicated AA	54	7.19 $\pm$ 0.973		

95% CI = 95% confidence interval

*S = significant difference

Table 3: Descriptive statistic of mean $\pm$ SD for CRP between complicated and noncomplicated AA

Parameters	Patient groups	Number of patients	Mean $\pm$ SD	P value	95% CI
CRP (ng/mL)	Complicated AA	36	0.528 $\pm$ 0.123	0.021*S	0.009–0.111
	Noncomplicated AA	54	0.468 $\pm$ 0.112		

95% CI = 95% confidence interval

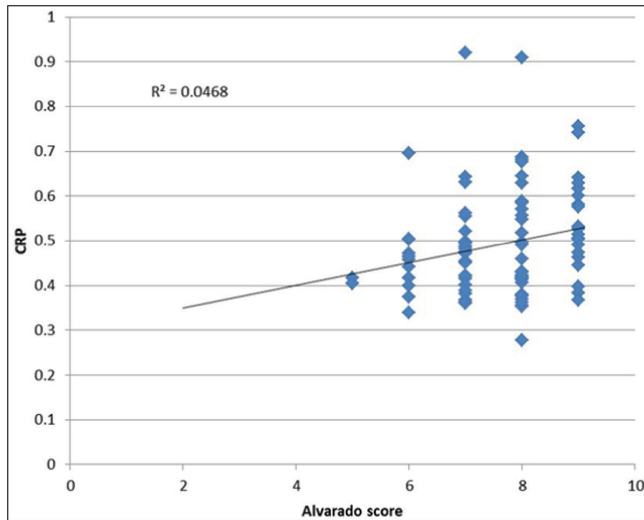
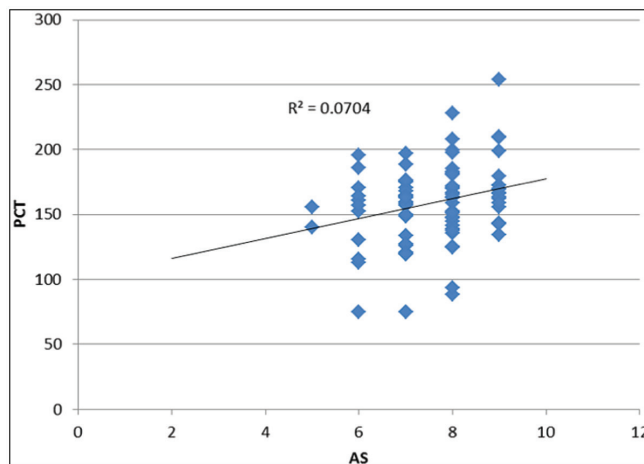
*S = significant

Table 4: Descriptive statistic of mean $\pm$ SD for PCT between complicated and noncomplicated AA

Parameters	Groups	Number of patients	Mean $\pm$ SD	P value	95% CI
PCT (pg/mL)	Complicated AA	36	176.438 $\pm$ 24.312	<0.001*S	17.656–39.701
	Noncomplicated AA	54	147.759 $\pm$ 27.766		

95% CI = 95% confidence interval

*S = significant

**Figure 2: Correlation between Alvarado score and CRP****Figure 3: Correlation between Alvarado score and PCT****Table 5: Correlation between Alvarado score and biochemical parameters**

	AS	PCT (pg/mL)	CRP (ng/mL)
AS	Pearson correlation (r)	0.265	0.216
	P value	0.012	0.040
	N	90	90
PCT (pg/mL)	Pearson correlation (r)		0.546
	P value		<0.001
	N		90

Alvarado score degree and concentrations of biochemical parameters CRP and PCT.

DISCUSSION

This study was supposed to be a cross-sectional study, involved 90 patients with AA, 54 patients with noncomplicated AA, and 36 patients with complicated AA. The mean age of complicated AA patient groups was 24.09 ± 8.401 years and that of noncomplicated AA patient groups was 26.64 ± 10.094 years. In this study, most of the cases (complicated and noncomplicated AA) fall within the age group of 15–35 years. That is due to the appendix tissue has characteristics of a lymphoid organ, and there is more lymphoid tissue in the young people. Any obstruction in the appendix lumen can produce lymphoid hyperplasia, which can progress to appendicitis if the condition is not treated. As a result, young people are more likely to develop appendicitis. These results are supported by research from around the world and were found in Lahore, Pakistan, where 66% of the population was between the ages of 15 and 30 years old.^[14]

The overall number of male patients in our study was 42 (46.7%), and the total number of female patients was 48 (53.3%), which agrees with Maral *et al.*'s, 2012 findings of a high incidence in females approximately (53.3%).^[15] Another finding agrees with our study: Hama Shareef *et al.* shown that females were 51.4% and males were 48.6%.^[16] Our study disagrees with the study in Al-Aziziyah Hospital in Wasit Governorate, which states that male to female ratio was 1.27:1 (56% males and 44% females),^[17] and also disagrees with the findings in other studies.^[18,19]

Alvarado scored appendicitis patients' clinical symptoms and utilized laboratory tests to divide them into three groups: patients with 7–10 points, who were highly suspected of having AA and required immediate surgery, patients with 0–4 points, who were discharged without further evaluation because of the low chances of having AA, and patients with 5–6 points, who were difficult to diagnose based on the scores alone.^[9] In our study, 13 patients (14.4%) had an Alvarado score of 5–6 points, and 77 patients (85.5%) had an Alvarado score of 7–10 points. As a result, we suggest that individuals with lower scores (less than 6) have nonspecific symptoms, resulting in a delayed diagnosis and a higher risk of developing complicated appendicitis.

CRP concentrations in the complicated AA patient group differed significantly ($P < 0.05$) from those in the non-complicated AA patient group, due to the fact that CRP is a biomarker that increases when inflammation progresses in the acute phase of many diseases. As a result, elevated CRP levels may help in predicting the detection of complicated appendicitis and assist in better surgical management.^[20]

A significant differences ($P < 0.05$) of PCT concentration in complicated AA patients group when compared with those of the non-complicated AA patients group these is due to PCT levels rise in response to a pro-inflammatory stimulus, particularly one of bacterial origin. As a result, it is frequently classified as an acute phase reactant.^[21] Blood levels of PCT can rise by multiple orders of magnitude as a result of the inflammatory cascade and systemic response that a severe infection causes, with higher values indicating more severe disease.^[22-24]

In this study, although it is weak, there is a statistically significant positive correlation between the Alvarado score degree and the concentration of CRP (P value = 0.040, $r = 0.216$), whereas the correlation between PCT and Alvarado score was relatively more positive than that between CRP and AS; also this correlation was statistically significant (P value = 0.012, $r = 0.0265$).

CONCLUSIONS

CRP and PCT support Alvarado score to differentiate between complicated AA and noncomplicated AA, and this is evident from the significantly higher concentrations of both in patients with complicated AA than in patients with noncomplicated AA, and this is consistent with the higher Alvarado score degree in patients of the first group; also the AUC, sensitivity, and specificity of PCT was higher than those of CRP. Therefore, it is more accurate in the diagnosis to support AS to differentiate between complicated and noncomplicated AA.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Kahai P, Mandiga P, Wehrle CJ, Lobo S. Anatomy, abdomen and pelvis, large intestine. In: StatPearls. StatPearls Publishing; 2021.
- Faisal L, Ajmal R, Rehman F, Islam Z, Qayyum SA, Athar S. Anatomical variations of vermiform appendix on plain MDCT and its association with acute appendicitis in adult urban population of

- Karachi, A tertiary care hospital experience. J Bahria Univ Med Dent Coll 2022;12:77-82.
- Vitetta L, Chen J, Clarke S. The vermiform appendix: An immunological organ sustaining a microbiome inoculum. Clin Sci (Lond) 2019;133:1-8.
- Lapsa S, Ozolins A, Strumfa I, Gardovskis J. Acute appendicitis in the elderly: A literature review on an increasingly frequent surgical problem. Geriatrics 2021;6:93.
- Ohle R, O'Reilly F, O'Brien KK, Fahey T, Dimitrov BD. The Alvarado score for predicting acute appendicitis: A systematic review. BMC Med 2011;9:139.
- Seudeal K, Abidi H, Shebrain S. Early versus delayed appendectomy: A comparison of outcomes. Am J Surg 2018;215:483-6.
- Federico C, Paola F, Massimo S, Enrico C, Maria GS, Gioacchino L, *et al.* Conservative treatment of acute appendicitis. Acta Bio Medica Atenei Parm 2018;89(Suppl 9):119.
- Di Saverio S, Podda M, De Simone B, Ceresoli M, Augustin G, Gori A, *et al.* Diagnosis and treatment of acute appendicitis: 2020 update of the WSES Jerusalem guidelines. World J Emerg Surg 2020;15:27.
- Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med 1986;15:557-64.
- Parekh D, Jain D, Mohite S, Phalgune D. Comparison of outer diameter of appendix, C-reactive protein, and serum bilirubin levels in complicated versus uncomplicated appendicitis. Indian J Surg 2020;82:314-8.
- Feng S, Lai X-H, Lou Y, Liu W. Diagnostic value of procalcitonin and C-reactive protein level for predicting appendiceal perforation in children. HK J Paediatr New Ser 2021;26:3-7.
- Kordass U, Carlson R, Stein VM, Tipold A. Measurements of C-reactive protein (CRP) and nerve-growth-factor (NGF) concentrations in serum and urine samples of dogs with neurologic disorders. BMC Vet Res 2016;12:1-8.
- Elabscience. Human PCT (Procalcitonin) ELISA Kit; 2015. p. 1-11.
- Aslam MN, Kamran A, Gondal KM, Andrabi I, Mahmood T, Ahmad M, *et al.* Appendectomy: A contemporary appraisal. Ann King Edward Med Univ 1999;5:184-7.
- Omar AS, Kadhim SJ. Accuracy of lintula score versus alvarado score in diagnosis of acute appendicitis in Al-yarmouk teaching hospital. Int J Surg 2020;4:18-23.
- Majrashi SA, Almalki M, Bardisi A. Retrospective study to explore a new predictor for the early diagnosis of perforated acute appendicitis. J Clin Case Stud 2018;3:11-3.
- Albahadili MA. Study of the effect of age, gender and seasonal variation on appendicitis in Azizyah-Iraq. Al-Kufa Univ J Biol 2016;8:7-12.
- Noudeh YJ, Sadigh N, Ahmadnia AY. Epidemiologic features, seasonal variations and false positive rate of acute appendicitis in Shahr-e-Rey, Tehran. Int J Surg 2007;5:95-8.
- Al-Omran M, Mamdani M, McLeod RS. Epidemiologic features of acute appendicitis in Ontario, Canada. Can J Surg 2003;46:263-8.
- Gharagozloo M, Kalantari H, Rezaei A, Maracy MR, Salehi M, Bahador A, *et al.* Clinical study: Immune-mediated cochleovestibular disease. Bratisl Lek Listy 2015;116:296-301.
- Dandonna P, Nix D, Wilson MF AA, Love J, Assicot MBC. Procalcitonin increase normal subjects. J Clin Endocrinol Metab 1994;79:1605-8.
- Sandkovsky U, Kalil AC, Florescu DF. The use and value of procalcitonin in solid organ transplantation. Clin Transplant 2015;29:689-96.
- Abbas ZA, El-Yassin HD. The impact of glycemic control on procalcitonin level in patients with type ii diabetes. Med J Babylon 2022;19:391-5.
- Hassan Y, Wani IA, Farooq SI. Mucocoele of appendix: A rare cause of surgical abdomen. Med J Babylon 2022;19:89-93.