

CRP versus Alvarado Score in Appendicitis Diagnosis

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Abstract... Objective: to evaluate whether C-reactive protein (CRP) level results on admission could aid the diagnostic accuracy of Alvarado score in patients with suspected appendicitis. **Study Design:** cross sectional study. **Study Place and Duration:** January to December 2019 in the Surgical Unit, Nishtar Hospital, Multan.

Methodology: Total 230 patients participated in the study with suspected acute appendicitis. Patient's Alvarado score, age of the patients, sex, length of period of complaint for abdominal pain and level of CPR were recorded on the time of admission. Descriptive statistics for study data included mean, median, standard deviation, minimum and maximum frequency and ratio values. Quantitative data was examined using Mann-Whitney U test. On the other hand a receiver operating characteristic curve was used for effects and cut-off values. **Results:** The mean C-reactive protein of AA complicated and AA uncomplicated patients was 40.61 ± 9.59 mg/L and 38.25 ± 9.08 mg/L, respectively. The difference was statistically insignificant, ($p=0.905$). The mean Alvarado score of AA complicated and AA uncomplicated patients was 7.51 ± 1.72 and 7.75 ± 2.08 , respectively. The difference was statistically insignificant, ($p=0.248$).

Conclusion: Serum levels of C-reactive protein when assessed alone are not adequate enough in making a diagnosis of acute appendicitis. When combined with Alvarado score, they increase the overall diagnostic value. Moreover these levels in serum also help in differentiation of uncomplicated and complicated acute appendicitis.

Keywords: Alvarado score, C-reactive protein, diagnostic accuracy, appendicitis

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INTRODUCTION

Acute pain represents one of the most common causes for consultation in the emergency department¹. Clinical diagnosis of appendicitis is often challenging even for experienced surgeons. Different disease processes mimic the diagnosis of acute appendicitis as there are a number of causes leading to pain in the right iliac fossa particularly in female patients^{2,3}. These difficulties likely contribute to the 28% to 57% rates of initially misdiagnosed appendicitis⁴. Recently, different clinical scoring systems aiding in the diagnosis of appendicitis have been developed. Alvarado score is one of the most commonly used scores⁵.

It provides measurably useful diagnostic information in evaluating suspected appendicitis. However, Alvarado score doesn't provide adequate predictive values to be used in clinical practice as the gold standard method for determination of the need for surgery⁶. Acute appendicitis is a common disease with an incidence of 42-175 in 100,000 persons⁷.

Nonetheless, because of its atypical symptoms and difficulties in making a definite diagnosis, only 84% of the patients who undergo an appendectomy manifest pathological findings of appendicitis⁸.

If it is diagnosed as simple appendicitis, the recovery time is relatively short without any complications. However, in perforated or gangrenous appendicitis due to the delay of operation, the hospital stay, the cost, and the incidence of early, as well as delayed, complications are increased drastically.

Therefore, it is no question that early detection and proper treatment for appendicitis enables to minimize postoperative complication⁹. Recently, the incidence of early diagnosis and treatment for acute appendicitis is high due to improvement of radiologic evaluation using computed tomography and ultrasonography, but the incidence of early detection for complicated appendicitis is still limited.

Currently, the diagnosis of complicated appendicitis depends on the onset of symptoms and physical examination; thus, inaccuracy due to subjective interpretation is common.

The aim of the study was to evaluate whether C-reactive protein (CRP) level results on admission could aid the diagnostic accuracy of Alvarado score in patients with suspected appendicitis.

Methodology

This is a cross sectional study. This study was done during January to December 2019 on the patients admitted in the Surgical Unit, for suspected acute appendicitis in Nishtar Hospital, Multan. Hospital, Medical Faculty Ethics Committee gave approval for the conduction of this prospective study. Total 230 patients participated in the study with suspected acute appendicitis, admitted to department of surgery and were agreed to the written consent for inclusion in the study. Sample size was calculated using the reference study by Dal et al [10]. Non-probability consecutive type of sampling technique was used to collect the sample size. The inclusion criteria for the study were to have people with age more than 18 years with complaints for more than 12 hours. On the other hand patients with age less than 18 years, who are pregnant, and had diseases like chronic renal failure, chronic viral disease, and autoimmune disease as well as not agreed to the written consent for the study were included in the exclusion criteria.

Patients were observed for 24 hours in which surgery was not performed. Patient’s Alvarado score, age of the patients, sex, length of period of complaint for abdominal pain and level of CPR were recorded on the time of admission. Peri-appendiceal area was irrigated, fluid samples were taken with 10 cc of normal saline and culture test was also performed. Patients that were monitored for 24 hours in the ward after first examination and discharged from hospital after reduction of complaints and those with normal appendix on observation after pathology evaluation were considered as acute appendicitis negative. While the patients reported to have appendicitis after histopathological examination were categorized as acute appendicitis positive. Patients with acute appendicitis positive histopathologically were further sub-classified into complicated and uncomplicated acute appendicitis cases including gangrene or perforated appendicitis and phlegmonous appendicitis respectively. CRP sensitivity was determined by the threshold level of 5mg/L. patients were considered acute appendicitis positive with an AS of greater than 7 while acute appendicitis negative patients were considered to be having an AS of less than 7.

Descriptive statistics for study data included mean, median, standard deviation, minimum and maximum frequency and ratio values. Quantitative data was examined using Mann-Whitney U test. On the other hand a receiver operating characteristic curve was used for effects and cut-off values. Statistical Package for the Social Sciences (SPSS, Version 23.0) for Windows was used for the statistical analysis. A P value of ≤ 0.05 was regarded as statistically significant.

Results

Two hundred and thirty patients were included in this study, both genders. There were n=132 (57.4%) males and n=98 (42.6%) females. The mean age of the patients was 34.44 ± 6.61 years. The mean abdominal pain, Alvarado score and C-reactive protein of the patients was 53.44 ± 3.61 hours, 7.89 ± 2.09 and 38.19 ± 9.23 mg/L, respectively. Acute appendicitis was positive in n=142 (61.7%) patients and negative in n=88 (38.3%) patients. The distribution of clinic and histopathology was observed as atypical acute appendicitis in n=31 (13.5%) patients, phlegmonous AA+AA in n=112 (48.7%) patients, negative appendectomy in n=9 (3.9%) and other pathologies in n=78 (33.9%) patients. (Table I).

The mean age of AA (+) and AA (-) patients was 34.74 ± 3.48 years and 33.96 ± 3.76 years, respectively. The difference was statistically insignificant, (p=0.444). The mean abdominal pain of AA (+) and AA (-) patients was 45.6 ± 4.74 hours and 67.04 ± 6.41 hours, respectively. The difference was statistically significant, (p=0.003). The mean C-reactive protein of AA (+) and AA (-) patients was 44.82 ± 2.98 mg/L and 27.48 ± 4.72 mg/L, respectively. The difference was statistically significant, (p=0.000). The mean Alvarado score of AA (+) and AA (-) patients was 7.95 ± 1.88 and 7.79 ± 2.41 , respectively. The difference was statistically significant, (p=0.020). (Table II).

The mean age of AA complicated and AA uncomplicated patients was 33.51 ± 3.87 years and 34.54 ± 11.96 years, respectively. The difference was statistically insignificant, (p=0.579). The mean abdominal pain of AA complicated and AA uncomplicated patients was 53.87 ± 10.74 hours and 54.51 ± 11.96 hours, respectively. The difference was statistically insignificant, (p=0.110). The mean C-reactive protein of AA complicated and AA uncomplicated patients was 40.61 ± 9.59 mg/L and 38.25 ± 9.08 mg/L, respectively. The difference was statistically insignificant, (p=0.905). The mean Alvarado score of AA complicated and AA uncomplicated patients was 7.51 ± 1.72 and 7.75 ± 2.08 , respectively. The difference was statistically insignificant, (p=0.248). E. coli positive in complicated AA of n=14 (45.2%) patients and E. coli negative in uncomplicated of n=28 (25%) patients. The difference was statistically significant (p=0.029). (Table III).

The classification of Alvarado score, CRP and AS+CRP with sensitivity, specificity, positive predictive value and negative predicted value were calculated in table. IV. The differences were statistically significant. (Table IV).

Table-I: Demographic and clinical characteristics of the patients

Variable	Presence
Gender	
Male	n=132 (57.4%)
Female	n=98 (42.6%)

Age (years)	34.44±6.61
abdominal pain (hours)	53.44±3.61
Alvarado score	7.89±2.09
C-reactive protein(mg/L)	38.19±9.23
Acute appendicitis	
Positive	n=142 (61.7%)
Negative	n=88 (38.3%)
Clinic and histopathology	
Atypical acute appendicitis	n=31 (13.5%)
Phlegmonous AA+AA	n=112 (48.7%)
Negative appendectomy	n=9 (3.9%)
Other pathologies	n=78 (33.9%)

Table-II: Comparison of acute appendicitis with clinical presentations

Variable	Acute appendicitis		P-value
	Positive n=142 (61.7%)	Negative n=88 (38.3%)	
Age (years)	34.74±3.48	33.96±3.76	0.444
Gender			
Male	n=75 (52.8%)	n=57 (64.8%)	0.075
Female	n=67 (47.2%)	n=31 (35.2%)	
Abdominal pain (hours)	45.6±4.74	67.04±6.41	0.003
C-reactive protein (mg/L)	44.82±2.98	27.48±4.72	0.000
Alvarado score	7.95±1.88	7.79±2.41	0.020

Table-III: Association between acute appendicitis and other variables

Variable	Acute appendicitis		P-value
	Complicated n=31 (13.5%)	Uncomplicated n=112 (48.7%)	
Age (years)	33.51±3.87	34.54±11.96	0.579
Gender			
Male	n=16 (51.6%)	n=64 (57.1%)	0.583
Female	n=15 (48.4%)	n=48 (42.9%)	
Abdominal pain (hours)	53.87±10.74	54.51±11.96	0.110
C-reactive protein (mg/L)	40.61±9.59	38.25±9.08	0.905
Alvarado Score	7.51±1.72	7.75±2.08	0.248
E. coli (+)	n=14 (45.2%)	n=28 (25%)	0.029
E. coli (-)	n=17 (54.8%)	n=84 (75%)	

Table-IV: Sensitivity and Specificity of CRP and Alvarado score

		AA (-)	A (+)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P-value
AS	≤7	56	55	69.3	91.2	93.2	59.6	0.00
	>8	32	87					
CRP (mg/L)	≤5	8	18	73.5	49.3	67.5	55.8	0.00
	>5	80	124					
CRP+AS	(-)	52	56	95.4	50.5	72.3	76.5	0.00
	(+)	36	86					

AS: Alvarado score, CRP: C-reactive protein

Discussion

In our study it was reported that levels of C-reactive protein (CRP) were not able to help in accurate diagnosis of the acute appendicitis. It is difficult to diagnose appendicitis, even after extensive research. Many recent studies reported different scoring systems to improve the accuracy in diagnosis of appendicitis¹¹. These scoring systems help differentiating the patients with immediate need of surgical care from those in which further observations may be beneficial. Alfredo Alvarado and Madan Samuel developed two appendicitis scores with the clear principle of appendicitis diagnosis¹².

Studies showed that for diagnosis of acute appendicitis Alvarado was considered to be reproducible diagnostic tool which is more practical and simple¹³. Less chances of negative appendectomy and delay in therapy was solved by the use of this scoring tool¹⁴. Though, some studies suggested that the scores provided by the Alvarado scoring tool were not enough to predict the need of surgical procedure in the patients¹¹. For the diagnosis of the appendicitis in the children WBC count (inflammatory marker), CRP and other serum markers were also considered.

Inflammatory conditions may be present in other conditions too, due to which inflammatory markers are not reliable for making a decision by surgeons whether to confirm the appendicitis or not¹⁵⁻¹⁹. Previous few studies concluded that when compared to CRP value, US is more helpful in diagnosis of acute appendicitis because it is low in price and do not use ionizing radiation, anesthesia, or contrast injections. US is a widespread diagnostic tool, used initially in the case of suspected appendicitis specially in children²⁰. The sensitivities related to the use of ultrasound for accurate diagnosis of appendicitis range from 71-92% while specificities range from 96-98%²¹.

In a study conducted by Toprak et al²², Alvarado score was used in combination with the US findings for the determination of the high or low probability of appendicitis in the patients. Findings from imaging techniques such as ultrasonography were proposed to be very helpful in diagnosis of the acute appendicitis.

AS has been used more often by many researchers and was a focus of interest since its introduction. In a study by Douglas et al²³, surgical procedure was not done in patients with AS of ≤ 4 . Similarly Winn et al²⁴, in his study, discharged twelve patients with AS of ≤ 4 and suggested that patients with AS of ≤ 4 did not require surgery. Four patients underwent surgery when presented again but did not diagnose appendicitis. Alvarado et al²⁵ suggested in his study that upto 80% of the patients with AS of < 6 had negative appendectomy. In a study by Khan et al²⁶ 4 patients were discharged as they had AS of ≤ 4 while 3 of these patients applied for treatment again and on examination it was observed that they had AS at 7 so surgery was done in these patients. Most of the studies suggested that patients were discharge at AS ≤ 4 while there are few studies suggesting surgical treatment for such patients.

There are diverse treatment approaches for the patients with AS of 5 to 7 in the literature. In the study by Winn et al²⁴ out of 52, he treated 49 patients having AS of 5-7 with antibiotics. While 27 of these 49 patients applied for treatment again and among these 10 underwent surgery. Similarly in study by Khan et al²⁶ 22 out of 31 patients with AS of 5-7 were discharged after 24 hours period of follow-up, and the remaining 9 patients underwent surgery (AA was confirmed in 6 of these patients).

In a study by Albu et al²⁷, it was proposed that 56 patients when pre-examined for acute appendicitis had a serum CRP level of 2.5mg/L. 100% sensitivity, 84.6% specificity, 86.6% positive predictive value, and 100% negative predictive value was reported for CRP and they argued that in case of CRP level less than 2.5mg/L surgery can be delayed. The positivity rate (10 mg/L and 12 mg/L) reported by Peltola²⁸ and Mikaelsson²⁹ was 72% and 47% respectively, for patients with suspected acute appendicitis. Some researchers agree on the fact that CRP levels are more helpful in predicting the complicated types of appendicitis. In a study by Yang et al²⁰ surgery was performed in 897 patients having suspected acute appendicitis. He reported that CRP value for these patients was 24.1mg/L and 96.8mg/L in cases of inflammatory appendicitis and perforated appendicitis, respectively. In a study conducted by the Pruekprasert et al³¹, he reported that 231 patients CRP level had sensitivity of 62% and specificity of 56%. CRP level was used in combination to AS in this study for diagnosing acute appendicitis. It was concluded that when used with AS the diagnostic value of CRP is increased for clinical diagnosis of acute appendicitis.

Conclusion

Serum levels of C-reactive protein when assessed alone are not adequate enough in making a diagnosis of acute appendicitis. When combined with Alvarado score, they increase the overall diagnostic value. Moreover these levels in serum also help in differentiation of uncomplicated and complicated acute appendicitis.

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