ORIGINAL ARTICLE

Diagnostic Accuracy of Lactate and C-reactive Protein in patients with acute appendicitis

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ABSTRACT

Aim: To determine the diagnostic accuracy of Plasma lactate and C-reactive protein in patients with acute appendicitis taking histopathology as gold standard.

Methodology: This study was conducted in department of Chemical Pathology, PGMI Lahore. Duration of study was one year. 200 suspected cases of acute appendicitis were included. Patients were categorized as with and without acute appendicitis on the basis of Lactate and c- reactive protein levels taking histopathology as gold standard. Sensitivity, specificity, positive predictive value, negative predictive value of Lactate and C-reactive protein were calculated.

Results: The mean plasma lactate levels were higher in patients with acute appendicitis when compare with subjects with no histological evidence of acute appendicitis, ($p < 0.001$). The sensitivity and specificity of Lactate assessed by ROC curve analysis were 90.9% and 91.7%, respectively. In 60 cases with appendicitis 57(95%) had CRP ≥ 6 mg/dl while 3(5%) had CRP level < 6mg/dl. In 60 cases without appendicitis 6(10%) cases had CRP ≥ 6mg/dl and 54(90%) cases had < 6 mg/dl CRP. There was a significant difference in the frequency of raised CRP levels (≥6) among cases with and without appendicitis, p-value ≤0.001. The sensitivity, specificity, positive predictive value and negative predictive value of CRP for diagnosis of acute appendicitis were 95%, 90% and 95%, respectively.

Conclusions: The Lactate and CRP have a good diagnostic accuracy for acute appendicitis and can be used as an alternate in patients suspected of acute appendicitis.

Keywords: Appendicitis, Diagnostics trail, C-reactive protein, Lactate, Histopathology

INTRODUCTION

About 7-10% of general population develops acute appendicitis with maximum incidence being in the 2nd and 3rd decades of life[1,2]. Appendicitis is the commonest surgical emergency presenting with abdominal pain and is the most common indication for emergency operation worldwide with approximately 250,000 appendectomies per year in developed countries[3]. The negative appendectomy rate is still about 15 percent and the perforation rate can be as high as 35 percent. Despite the wide use of imaging techniques, appendicitis remains a challenging diagnosis[4]. The ability of computerized tomography to reduce the rate of negative appendectomies and perforations is still under discussion and remains to be proved in prospective trials[5]. Clinical experience remains of major importance in diagnosing acute appendicitis. The Alvarado score is a simple, easy scoring system at both end of scale. But the sensitivity of Alvarado score was 58.2% and specificity was 88.9%[6]. In spite of the widespread use of various advanced diagnostic tools, the diagnosis of appendicitis is not always easy to make. To support the diagnosis of appendicitis, leukocyte counting and C-reactive protein have been investigated in different studies[7,8]. For plasma lactate taking cutoff at 8mg/dl, the sensitivity, specificity, PPV and NPV were 80%, 53%, 77% and 57% and for C-reactive protein at cutoff of 7.4 U/L, the sensitivity, specificity, PPV and NPV were 83%, 93%, 96% and 73%, respectively[9]. Another study reported sensitivity, specificity, PPV and NPV of C-reactive protein was 90.0%, 74.3%, 79.8% and 74.3% respectively[10]. Another study found that lactate had a high sensitivity (100%) and specificity (83%) in determination of cause of acute abdominal disorder[11]. Filiz and colleagues found the lactate as 97% sensitivity, 93% specificity, 90% PPV and 95% NPV, and 95% accuracy[12]. The aim of this study was to assess diagnostic accuracy of serum CRP and lactate for preoperative diagnosis of AA thus avoiding unnecessary surgical intervention.

METHODOLOGY

The study was done at Lahore general hospital from 2014 to 2016. Blood samples of a total 200 suspected cases of acute appendicitis of either sex having age range 18 to 55 years were assessssed for plasma lactate and C-reactive protein following standard laboratory protocol. Lactate was determined by chemistry analyzer using enzymatic method and C-reactive protein concentration was determined by latex agglutination slide test method in undiluted serum. All the instructions were followed according to manufacturer. Calibration curve was made. Controls were run to ensure the analytical precision and accuracy. The patients were labeled as having confirmed diagnosis of acute appendicitis based on presence of neutrophil count (>5/HPF) in

mucosa, submucosa and muscularis with congestion of subserosal vessels and perivascular neutrophil emigration on histopathological findings postoperatively. All the collected data was entered and analyzed into SPSS version 20.

RESULTS

The mean age of patients was 23.70±7.27 (18-50) years. There were 142(71%) male and 58(29%) female cases. The mean duration of pain was 7.87±1.89 (4-12) hours. The mean Alvarado score was 8.42±0.54 in this study. The mean plasma lactate was 10.53±2.76 mg/dl (5.80–17.20) as presented in table 1. There were 116 cases which were positive on both histopathology and plasma lactate while 48 cases were negative on both histopathology and plasma lactate. There 32 false positive and 4 false negative. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of plasma lactate was 96.67%, 60%, 78.38%, 92.31% and 82% respectively as presented in table 2.

In 148 cases with positive appendicitis 140(95%) had CRP ≥ 6 while 8(5%) had CRP level < 6. In 52 cases with negative appendectomy 5 (10%) cases had CRP ≥ 6 and 47(90%) cases had < 6 CRP. There was significant association between CRP level (≥6) and positive histological confirmed cases, p-value ≤0.001 as presented in table 3. The sensitivity, specificity, PPV and NPV of C-reactive protein were 96.55%, 85.45%, 94.59%, 90.38% respectively.

Table 1: Descriptive Statistics of quantitative variables

	Age (years)	Duration of Pain(hrs)	Alvarado score	Plasma Lactate mg/dl
Mean	23.70	7.87	8.42	10.53
S.D	7.27	1.89	0.54	2.76
Range	32.00	8.00	3.00	11.40
Minimum	18.00	4.00	7.00	5.80
Maximum	50.00	12.00	10.00	17.20

Table 2: Comparison of Plasma lactate and histopathological findings

Plasma Lactate(mg/dl)	Histopathological findings		Total
	Positive	Negative	
≥ 8	116	32	148
< 8	4	48	52
Total	120	80	200

Table 2: Comparison of C-reactive protein and histopathological findings

C-reactive protein(mg/dl)	Histopathological findings		Total
	Positive	Negative	
≥6	140	8	148
< 6	5	47	52
Total	145	55	200

DISCUSSION

Acute appendicitis is affecting almost 7% of the urbanized population, with an incidence of 1.1 cases per 1000 people per year[13]. In Pakistan, it was found in a study that total of 75 patients presented with acute abdominal pain. Out of them 36(48%) were diagnosed as acute appendicitis[14]. One study reported that out of 200 patients, 160(80%) underwent appendesectomy and 137(85.8%) were confirmed having acute appendicitis on histopathological examination[15]. Acute appendicitis needs to be considered in the differential diagnosis of all patients with abdominal pain. A high index of suspicion is necessary to guard against misdiagnosis, especially in the elderly. Delays in presentation and diagnosis are associated with higher rates of perforation and, hence, higher morbidity. Repeated clinical examination, a high index of suspicion and urgent investigations are necessary for a correct and rapid diagnosis. 14 The combination of pain in right iliac fossa, anorexia, leukocytosis and fever is classic presentation[16]. Serum markers for the diagnosis of acute appendicitis would be of great diagnostic value as a non-invasive test method[17]. Many attempts have been made to determine ways of decreasing the negative findings after a clinical suspicion of acute appendicitis[18]. One study reported CRP concentration of 12.74±7.92 mg/dl in patients with appendicitis 9. This coincides with the results from my current study in which increased CRP levels (>6mg/dl) in most of the patients of appendicitis was observed. Quantitative method of CRP was not used in current study but adopted the cut off value at 6mg/dl to differentiate positive and negative appendix. The results showed that 95% of the patients of acute appendicitis had raised CRP levels. In contrast to this, in patients with negative appendectomy only 10% had raised CRP levels. These results point to a strong association between raised CRP levels and acute appendicitis, p-value ≤0.001.

C-reactive protein (CRP) is now frequently used to guide clinical judgments and past studies have demonstrated specificities of CRP measurements ranging from 38–87% and sensitivities of 40% to 94%[19,20]. A recent study in 2016 reported high sensitivity of raised CRP as 93.3% and specificity of 86.6% in diagnosing acute appendicitis[21]. Most of the studies mentioned in literature favor the results of my current study. It is believed that CRP is an acute phase protein and is increased when there is a tissue injury. The levels peak in 24-48 hours following tissue insult and remain elevated till the infection or tissue destruction persists[22]. This forms the basis of using CRP as an indicator of acute appendicitis.

In my current study, higher level of plasma lactate was found i.e. plasma lactate level in patients with appendicitis was 12.32 ± 1.97 mg/dl and in subjects with negative AA was 7.92±1.12 mg/dl. The mean Plasma lactate level was higher in patients with AA when compare with subjects without AA, p-value < 0.001. My study findings are in agreement with the study by (Kavakli et al., 2010) in which they reported that lactate level was 10.70±3.94 mg/dl in patients with acute appendicitis and 7.83±1.74 mg/dl in patients without acute appendicitis (p<0.001 for lactate).9 Most of the studies are done to identify the best cut-off point as one study reported that for plasma lactate taking cutoff at 8 mg/dl, the sensitivity, specificity, PPV and NPV were 80%, 53%, 77% and 57% and for C-reactive protein at cutoff of 7.4 U/L, the sensitivity, specificity, PPV and NPV were 83%, 93%, 96% and 73%, respectively. 9 Another study found that lactate had a high sensitivity (100%) and specificity (83%) in determination of cause of acute abdominal disorder.11Filiz

and colleagues found the lactate as 97% sensitivity, 93% specificity, 90% PPV and 95% NPV, and 95% accuracy. 12 These results point towards the utility of plasma lactate levels in diagnosis acute abdominal conditions such as acute appendicitis. The possible explanation to this increase in the lactate levels is attributed to the fact that low oxygen tension in acute abdominal conditions lead to an increase in lactate levels[23]. Hence it is suggested that CRP measurement and lactate levels must be adopted as a regular laboratory investigations in patients with suspected diagnosis of acute appendicitis.

CONCLUSION

The lactate and c- reactive protein have a good diagnostic accuracy for acute appendicitis and can be used as an alternate tool for diagnosis in patients suspected of acute appendicitis and unnecessary surgical intervention can be prevented.

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