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## C – REACTIVE PROTEIN; IN PATIENTS WITH ACUTE APPENDICITIS

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**ABSTRACT...** Acute appendicitis is the most common abdominal surgical emergency despite advances in radiographic imaging and diagnostic laboratory investigations; the diagnosis of acute appendicitis remains challenge. **Objectives:** To evaluate the C-reactive protein in patients with acute appendicitis. **Patients and methods:** This cross sectional descriptive study of six months study was conducted at Liaquat University Hospital Hyderabad. All the patients with acute appendicitis were admitted in the ward and were further evaluated for C-reactive protein. The data was analyzed in SPSS 16 and the frequency and percentage was calculated. **Results:** One hundred subjects with acute appendicitis were recruited and studies. The mean age  $\pm$ SD of the patients was  $27.83 \pm 07.52$  in overall population while it was  $29.73 \pm 06.64$  and  $25.84 \pm 04.92$  in male and female subjects with acute appendicitis. The CRP was raised in 60% patients. The distribution of age in relation to gender and CRP was statistically significant ( $p = 0.01$  and  $<0.01$ ) whereas the CRP was also observed as statistically significant in context to gender and histopathology ( $p = 0.02$  and  $0.03$ ) respectively. The mean  $\pm$ SD of CRP was  $7.53 \pm 1.52$  in overall population while it was  $6.84 \pm 1.64$  and  $8.65 \pm 1.53$  in male and female patients with raised CRP. **Conclusions:** The CRP was elevated in patients with acute appendicitis.

**Key words:** CRP, appendicitis, C-reactive protein, inflammatory marker and acute phase protein

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### INTRODUCTION

Acute appendicitis is the most common abdominal surgical emergency despite advances in radiographic imaging and diagnostic laboratory investigations; the diagnosis of acute appendicitis remains challenge<sup>1</sup>. Appendectomy is the most common cause of acute surgical abdomen with a lifetime risk of 7%<sup>2</sup>. The specific clinical and laboratory findings usually play a major role in diagnosis and treatment, whereas few subjects have different and atypical presentations leading to misdiagnosis<sup>3</sup>. This is common in women of childbearing age, in the paediatric and elderly age groups<sup>4</sup>. The diagnosis may be easy but may also be very difficult and often wrongly made as initially overlooked, the former leading to unnecessary surgery and the latter to delay the illness period<sup>5</sup>. Diagnostic difficulty in patients with atypical clinical findings resulted in unnecessary appendectomies and had been variably reported in the surgical literature to be between 08% and 33% with an average of about 20%<sup>6,7</sup>. Although the

rate of negative appendectomies rises to 35% to 45% in young women of childbearing age in whom differential diagnosis of pelvic inflammatory diseases may be difficult<sup>8</sup>.

C - reactive protein (CRP) is an acute phase reactant and rises rapidly in response to tissue injury, infection and inflammation, and can be measured in serum after the onset of inflammatory reaction<sup>9,10</sup>. Former literature had investigated the role of CRP in evaluating the diagnosis of acute appendicitis with promising results. Asfar S, et al, have found that CRP was raised in 72% patients with acute appendicitis and had specificity and sensitivity of 86.6% and 93.6% respectively<sup>11</sup>.

In our tertiary care teaching hospital, acute appendicitis remains the most common acute abdominal emergency warranting surgery. The cases presented with atypical clinical manifestation the diagnosis become difficult.

Because easy availability and cost effectiveness, the CRP plays a definitive role in the diagnosis of subjects with suspected acute appendicitis and helps in reducing the number of negative laparotomies. Until now, in our hospital no one has done a study to observe the role of CRP in acute appendicitis. Therefore, this study was intended to evaluate the importance of inflammatory marker to evaluate the severity and diagnosis of acute appendicitis.

## PATIENTS AND METHODS

This study was conducted on patients,  $\geq 15$  years age, either gender, attended the outpatient clinic / ward of department of General Surgery and Emergency at Liaquat University Hospital Hyderabad with the complain of pain in the right lower abdomen from March 2013 to August 2013 were enrolled and entered in the study. The detail history and relevant physical examination was done to workup for acute appendicitis. Patients with co-morbid conditions were managed conservatively and patients with alternative diagnoses who were treated with other medical or surgical modalities were also excluded from the study. Clinical diagnosis of acute appendicitis was done by the collaboration and mutual case-discussion by our research teams that consist of consultant surgeons on the basis of symptoms of pain, migration, nausea and vomiting, anorexia, fever and signs of peritoneal inflammation like right iliac fossa tenderness, rebound tenderness and guarding. Once acute appendicitis was suspected, patient was subjected to routine investigations as per the hospital protocol. Total leukocyte count and differential count was advised in all subjects. Ultrasonography of abdomen was done in most of the cases to rule out the alternative diagnoses. Serum C-reactive protein estimation was advised in all these cases and the specimen was tested within one hour of collection by taking 02cc venous blood sample in a disposable syringe and sent to laboratory for analysis. The normal reference range for C-reactive protein is 0-1.0 mg/dl while the level  $>1.0$  mg/dl was considered as raised. Patients with strong suspicion of acute appendicitis were advised emergency appendectomy,

therefore after obtaining consent they were operated and the appendectomy specimen was sent for histopathological examination. The histopathology report was considered as the final diagnosis and to evaluate the severity of inflammation.

The patients were carefully monitored during the post-operative period for any complications. All patients were followed up in the outpatient department for a period of two months. The data was collected on predesigned proforma and was entered, saved and analyze in SPSS version 16. The frequency and percentage was calculated for C-reactive protein in patients with acute appendicitis and for age and gender distribution. The mean  $\pm$  SD calculated for numerical variables. The stratification was done for age, gender, C-relative protein, leukocyte count and histopathology and the chi-square test was applied on categorical variables at 95% confidence interval and the p-value  $\leq 0.05$  was considered as statistical significant.

## RESULTS

One hundred subjects with acute appendicitis were recruited and studies. The mean age  $\pm$ SD of the patients was  $27.83 \pm 07.52$  in overall population while it was  $29.73 \pm 06.64$  and  $25.84 \pm 04.92$  in male and female subjects with acute appendicitis. The mean  $\pm$ SD of CRP was  $7.53 \pm 1.52$  in overall population while it was  $6.84 \pm 1.64$  and  $8.65 \pm 1.53$  in male and female patients with raised CRP. Regarding symptoms the pain in abdomen was observed in all subjects, anorexia was identified in 82 patients, diarrhea / vomiting was detected in 70 patients, fever was found in 67 individuals while 30 subjects had combined and others symptoms. Regarding the signs, rebound tenderness was observed in 80% patients, guarding in 60% subjects, tachycardia in 58% patients while the temperature and others signs was observed in 78% and 25% patients with acute appendicitis. The Alvarado score  $\geq 07$  was found in 94% patients while the 06 patients had  $<07$  score. The CRP was raised in 60% patients and during post operative period a directly proportional association was observed in recovery

and the serum CRP level. The age in relation to gender, leukocytosis and CRP is shown in Table I-III while the gender in relation to leukocytosis

and CRP is shown in Table-IV and V whereas the gender and CRP in relation to histopathology is shown in Table VI-VII.

		GENDER		Total	P-value
		Male	Female		
AGE	15-19	21	2	23	0.01*
		31.3%	6.1%	23.0%	
	20-29	25	23	48	
		37.3%	69.7%	48.0%	
	30-39	13	6	19	
		19.4%	18.2%	19.0%	
	40-49	6	1	7	
		9.0%	3.0%	7.0%	
	50 +	2	1	3	
		3.0%	3.0%	3.0%	
Total		67	33	100	
		100.0%	100.0%	100.0%	

Table-I. The distribution of age in relation to gender

\*P-value is statistically significant

Pearson Chi-square value = 12.10; df = 4

		Leukocytosis		Total	P-value
		Yes	No		
AGE	15-19	17	6	23	0.04*
		29.8%	14.0%	23.0%	
	20-29	25	23	48	
		43.9%	53.5%	48.0%	
	30-39	8	11	19	
		14.0%	25.6%	19.0%	
	40-49	6	1	7	
		10.5%	2.3%	7.0%	
	50 +	1	2	3	
		1.8%	4.7%	3.0%	
Total		57	43	100	
		100.0%	100.0%	100.0%	

Table-II. The distribution of age in relation to leukocyte

\*P-value is statistically significant

Pearson Chi-square value = 7.91; df = 4

**DISCUSSION**

Appendicitis is a common abdominal surgical emergency and appendectomy is one of the most frequently performed abdominal operations<sup>12</sup>. The negative explorations and burden faced not only by the general surgeon, but also the patient and the society as a whole, since appendectomy, like any other operations

results in socio-economic impacts in the form of hospital expenses, lost working days, and declined productivity<sup>13</sup>.

In present study pain abdomen, anorexia and vomiting are the predominant clinical symptoms but in reality they are not specific and relevant features as far as acute appendicitis is concerned

		CRP		Total	P-value
		Raised	Normal		
AGE	15-19	21	2	23	<0.01*
		35.0%	5.0%	23.0%	
	20-29	20	28	48	
		33.3%	70.0%	48.0%	
	30-39	13	6	19	
		21.7%	15.0%	19.0%	
	40-49	4	3	7	
		6.7%	7.5%	7.0%	
	50 +	2	1	3	
		3.3%	2.5%	3.0%	
Total		60	40	100	
		100.0%	100.0%	100.0%	

**Table-III. The distribution of age in relation to CRP**

*\*P-value is statistically significant*

*Pearson Chi-square value = 16.75; df = 4*

		Leukocytosis		Total	P-value
		Yes	No		
GENDER	Male	33	34	67	0.02*
		57.9%	79.1%	67.0%	
	Female	24	9	33	
		42.1%	20.9%	33.0%	
Total		57	43	100	
		100.0%	100.0%	100.0%	

**Table-IV. The distribution of gender in relation to leukocyte**

*\*P-value is statistically significant*

*Pearson Chi-square value = 16.75; df = 1*

		CRP		Total	P-value
		Raised	Normal		
GENDER	Male	35	32	67	0.02*
		58.3%	80.0%	67.0%	
	Female	25	8	33	
		41.7%	20.0%	33.0%	
Total		60	40	100	
		100.0%	100.0%	100.0%	

**Table-V. The distribution of gender in relation to CRP**

*\*P-value is statistically significant*

*Pearson Chi-square value = 5.09; df = 1*

although migration of pain identified in 90% cases is more specific symptom for acute appendicitis. The presence of fever assists the diagnostic accuracy. Tachycardia commonly seen in patients with acute appendicitis may also be seen in many other disorders. Right iliac fossa tenderness is

present in all cases, but is not specific for acute appendicitis. Rebound tenderness and guarding if present, are more specific for acute appendicitis and observed in 80% and 60% in present study, the observation is consistent with the study by Ngowe NM, et al<sup>14</sup>.

		Histopathology		Total
		Inflamed appendix	Normal	
GENDER	Male	49	18	67
		62.8%	81.8%	67.0%
	Female	29	4	33
		37.2%	18.2%	33.0%
Total		78	22	100
		100.0%	100.0%	100.0%

**Table-VI. The distribution of gender in relation to histopathology**

*\*P-value is statistically significant*

*Pearson Chi-square value = 2.80; df = 1*

		Histopathology		Total	P-value
		Inflamed appendix	Normal		
CRP	Raised	51	9	60	0.03*
		65.4%	40.9%	60.0%	
	Normal	27	13	40	
		34.6%	59.1%	40.0%	
Total		78	22	100	
		100.0%	100.0%	100.0%	

**Table-VII. The distribution of CRP in relation to histopathology**

*\*P-value is statistically significant*

*Pearson Chi-square value = 4.28; df = 1*

In current series Leucocytosis is present in 57% patients with acute appendicitis but also found to be raised in other inflammatory and infectious conditions as well so can be comparable with other studies done formerly. Doraiswamy, in his study reported leucocytosis in 42% patients and neutrophilia in 96%<sup>15</sup>. The observation was also detected by Hyman P, et al and Kim-Choy NG, et al<sup>16,17</sup>.

The Alvarado score is a 10-point scoring system based on clinical signs and symptoms and a differential leucocyte count<sup>18</sup>. Alvarado recommended an operation for all patients with a score of 7 or more and under observation for patients with scores of 5 or 6<sup>18</sup>. In our study, Alvarado score was  $\geq 07$  was observed in 94% patients suggestive of acute appendicitis underwent appendectomy and then the specimen was confirmed by histopathologically

In our study, serum CRP estimation in diagnosis of acute appendicitis yielded raised CRP in 60% patients with acute appendicitis and the finding is consistent with the study by Asfar, et al and

Pruekprasert, P et al<sup>11,19</sup>. Serum CRP is rapidly emerging as a diagnostic tool with proven use and being an acute phase reactant, CRP may be elevated in other conditions as well, and hence the specificity of CRP is low but it is a best inflammatory marker because of its dramatic rise in response to infection / inflammation and is always associated with pathological disorder<sup>20,21</sup>. CRP values have been found to rise on repeated testing, whereas WBC values decreased and CRP values when combined with clinical examination and leucocytosis will provide high diagnostic sensitivity and specificity as far as acute appendicitis is concerned<sup>22</sup>. Serum CRP estimation does not undermine the importance of clinical diagnosis by a skilled surgeon but can compliments it<sup>23</sup>.

Thus, at the end, it should be stressed that serum CRP estimation does not replace clinical diagnosis, but is useful adjunct diagnostic tool in acute appendicitis. Clinical diagnosis is crucial in ruling out alternate diagnoses and other disorders while serum CRP value should be correlated with clinical findings and leucocyte count. Sonography

is a useful tool if facilities are available, but adds to the cost of patient care. Therefore, this study proved the adjunct value of serum CRP estimation in suspected cases of acute appendicitis.

## CONCLUSIONS

Acute appendicitis remains a diagnosis based primarily on history and clinical examination while the CRP can compliment it and the present study found 60% predominantly male subjects with appendicitis had raised CRP and was statistically significant in relation to age, gender and histopathologically. Therefore, inflammatory variables like CRP contain valuable importance and should always be included in the diagnostic evaluation of acute appendicitis.

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"The only thing necessary for the triumph of evil is for good men to do nothing."

Edmund Burke (1729-1797)

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2	Dr. Shahnawaz Abro	Drafting the article and share its expert research opinion and experience in finalizing the manuscript	
3	Dr. Ashfaque Ahmed Bhurgiri	Connection and interpretation of data and give his expert view of manuscript designing	
4	Dr. Raheel Imtiaz Memon	Collection and acquisition of data, analysis and interpretation of data and make it suitable for final revision and corresponding author	
5	Dr. Syed Zulfiquar Ali Shah	Analysis and interpretation of data contributed in conception and shares its expert research opinion	