ORIGINAL ARTICLE

Socioeconomic, Laboratory and Associated Factors in Patients Suffering From Acute Appendicitis

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ABSTRACT

Background: Acute appendicitis (AA) is the most common clinical condition worldwide. In Pakistan, about 400,000 appendectomies are routinely carried out in surgical departments yearly. This study aims to find the latest and updated information regarding the diagnostic accuracy of CRP levels in AA. This will help surgeons make timely decisions, thus reducing the morbidity and mortality associated with complicated appendicitis.

Methods: This descriptive cross-sectional study was performed at KTH Peshawar from February to august 2018. It was designed to analyze C-reactive protein levels among acute appendicitis patients using positive and negative predictive values. Histopathologically confirmed appendicitis patients were included.

Results: In the current study, 216 patients suffering from Acute appendicitis were studied observed. The symptoms duration was < 2days in 75% patients while >2 days symptoms were found in 25% population. Majority patients were poor (46%), followed by middle class (42%), and rich (12%). Obesity was only observed in 22% patients suffering from AA. Diabetes and hypertension was observed in 18% and 15% patients respectively. Diagnostic accuracy of acute appendicitis was also calculated between CRP and Histopathology findings based on age, diabetes mellitus, gender, hypertension, obesity, and period of symptoms.

Conclusion: Our study concludes that the acute appendicitis symptoms appeared in less than two days. Acute appendicitis predominantly found in poor and middle class patients. Acute appendicitis should be diagnosed based mostly on its clinical symptoms. Despite the fact that CRP is a particularly helpful marker in the clinical diagnosis of acute appendicitis, general surgeons must apply their clinical judgement. The function of CRP in acute appendicitis should be examined in future research with a bigger sample size.

Keywords: C-reactive protein level, Socioeconomical factors, Acute Appendicitis, Diagnostic accuracy, Histopathological.

INTRODUCTION

Acute appendicitis (AA) is the most common surgical condition requiring emergency surgery worldwide[1,2]. According to Global burden of disease 2013, AA is the most common diagnosis in patients seeking medical help in the emergency room due to acute abdomen causing 72,000 deaths among 16 million cases reported globally[3]. The lifetime risk of AA is 16.33% for males and 16.34% for females in South Korea[4]. In Pakistan, about 400,000 appendectomies are routinely carried out in surgical departments each year[5]. Many laboratory investigations have been added over time in diagnosing appendicitis. The commonest is White Blood Cell Count, while others include C- Reactive Protein (CRP), Plasma Total Anti-Oxidant Capacity, Phospholipase A2, and Interleukin-6. All of these have been discussed in the view of current literature[6]. CRP is an acute-phase reactant synthesized by the liver in response to bacterial infection. Serum levels rise within 4 - 6 hours of acute tissue inflammation. A rapid assay is widely available[7]. Searching through the literature, we find many studies done on the subject. Most have explicitly advocated its role in diagnosing acute appendicitis, while others have supported a combination of CRP with other baseline investigations[8]. Bhopal FG et al. found that total leucocyte counts are the first-line indicator in any disease condition. Still, for the C-reactive protein, which is an acute phase protein and elevated level in the acute stage of the disease in acute appendicitis, the CRP level specificity and sensitivity in serum is 98% and 87.5% respectively, with predictive value test almost 98% and that negative test in the range of 87.5%[9,10]. Erythrocyte Sedimentation Rate (ESR) is another marker of inflammation[11]. Its levels are expected to rise in chronic infections. Authors have made debates in understanding the balance between CRP and ESR. They have found CRP superior to ESR in terms of rapidity of response and specificity for inflammation[12]. The CRP is more precise and reproducible and a quick test to perform than the ESR[13]. It is an acute phase reactant and a marker of inflammation or infection. CRP levels are elevated between eight to twelve hours after the onset of cellular response

processes, with a peak between 24 and 48 hours. Normal level = 0-6 mg/dl, Increased level = >6 mg/dl[14]. Acute appendicitis was diagnosed based on the presence of all of the following features: Unexpected onset of different signs and symptoms were examined, White cell count of ≥10000 cm^3 /dl on laboratory investigation[15]. Histopathological findings in acute appendicitis: can be grouped into: Group A: normal appendix, Group B: inflamed appendix (Focal acute inflammation in the mucosa), Group C: gangrenous appendicitis (Polymorph nuclear infiltration of the entire appendicular wall with the presence of necrosis), Group D: perforated appendix (Rupture of the appendicular wall to the serosal Surface)[16]. This study helps the timely diagnosis of acute appendicitis and provides baseline information on acute appendicitis. This aimed to determine C-reactive protein levels in acute appendicitis patients.

METHODOLOGY

Study Design, Setting and Duration: This cross-sectional study was performed at Khyber Teaching Hospital, Peshawar, from Feburary to August 2018.

Sample Size: The sample size was 216 taking a sensitivity of CRP of 85.1%, specificity of CRP of 72%[17], and prevalence of acute appendicitis of 22.71%[18] while a confidence interval of 95% and 10% margin of error.

Sampling Technique: Non-probability consecutive sampling.

Inclusion Criteria: All the patients with acute appendicitis, patientsof >18 years, either gender were included in the study.

Exclusion Criteria: Patients with conditions influencing CRP levels like autoimmune diseases, acute coronary syndrome, aortic aneurysm/dissection, acute cholecystitis, acute pancreatitis, pelvic inflammatory disease, chronic liver disease, pneumonia, burn injury, cancers and urinary tract infection etc.

Confonders: If included in the study, these patients may act as confounders; therefore, they were excluded.

Ethical Approval and Consent Form: Approval from the hospital ethical committee and CPSP research committee was achieved,

and all patients meeting inclusion criteria were approached after informed written consent.

Patients Data Collection Procedure: All 216 patients with acute appendicitis (as per operational definition) were included in the study through Out Patient Department (OPD) or Emergency room (ER) of Khyber Teaching Hospital. Peshawar. A questionnaire was designed regarding the age, gender, symptoms duration, obesity, diabetes mellitus, and hypertension.

Data Analysis: All the statistics were studied in SPSS 20. Continuous variables like diabetes mellitus, gender, and obesity, mean and standard deviation, were calculated as a period of symptoms and CRP. Frequencies and percentages were determined for categorical variables like hypertension, CRP and histopathology findings. CRP's diagnostic accuracy (sensitivity, specificity, positive predictive value, negative predictive value) was computed. It was stratified with age, gender, obesity, diabetes mellitus, hypertension and duration of symptoms to see the effect modifications. Post-stratification diagnostic accuracy was also computed. All the results were presented in the form of tables and graphs.

RESULTS

A total of 216 patients with acute appendicitis symptoms were studied. Among total, 75% (n=162) patients having a duration of symptoms < 2 days while 25% (n=54) patients had a duration of symptoms > 2 days were found (Table 1).

Table 1: Duration of symptoms in patients suffering from acute appendicitis

Duration	Frequency	Percentage
< 2 Days	162	75%
>2 Days	54	25%
Total	216	100%

Socioeconomic status among 216 patients was examined as 99(46%) patients were poor, 91(42%) patients were middle class and 26(12%) patients were rich (Table 2).

Table 2: Socioeconomic Status of patients suffering from acute appendicitis

Socioeconomic Status	Frequency	Percentage
Poor (Monthly Income <15,000 Rs)	99	46%
Middle Class (Monthly Income 15,000 - 50,000 Rs)	91	42%
Rich (Monthly Income >50,000 Rs)	26	12%
Total	216	100%

Obesity among 216 patients was examined as 48(22%) patients were obese, while 168(78%) patients were not obese (Table 3).

Table 3: Obesity In patients suffering from acute appendicitis

Obesity (Bmi >27 Kg/m^2)	Frequency	Percentage
Yes	48	22%
No	168	78%
Total	216	100%

The mean BMI was 26 Kg/m^2 with SD ± 3.43

Diabetes mellitus among 216 patients was analyzed as 39(18%) patients had diabetes while 177(82%) patients did not have diabetes (Table 4).

Table 4: Diabetes mellitus in patients suffering from Acute Appendicitis

Diabetes Mellitus	Frequency	Percentage
Yes	39	18%
No	177	82%
Total	216	100%

Hypertension among 216 patients was examined as 32(15%) patients were hypertensive, while 184(85%) patients were not hypertensive (Table 5).

Diagnostic accuracy of acute appendicitis concerning age, gender, obesity, diabetes mellitus, hypertension and period of symptoms (Table 6, 7, 8, 9, 10, 11, & 12).

Table 5: Hypertension in patients suffering from acute appendicitis

Hypertension	Frequency	Percentage
Yes	32	15%
No	184	85%
Total	216	100%

Table 6: CRP Vs Histopathology WRT Age Distribution (18-30 years and 31-45 years)

Parameters		Histopathology					
		18-30 Years			31-45 Years		
		+	-	Total	+	-	Total
CRP	+	A122 TP	B2 FN	124	A58 TP	B 1 FN	59
	-	C20 FP	D2 TN	22	C 9 FP	D 1 TN	10
	Total	142	4	146	67	2	69

Sensitivity=122/122+20* 100 = 122/142*100= 85.91%
Specificity = 2/2+2*100 = 2/4* 100= 50%
Positive prognostic value = 122/122+2* 100 = 122/124*100= 98.38%
Negative prognostic value = 2/2+20* 100 =2/22*100= 9%
Diagnostic Accurateness = 122+2/146 * 100 = 124/146* 100=84.93%

Table 7: CRP Vs Histopathology WRT Gender Distribution (Male and Female)

Parameters		Histopathology					
		Male			Female		
		+	-	Total	+	-	Total
CRP	+	A99 TP	B2 FN	101	A80 TP	B2 FN	82
	-	C 16 FP	D2 TN	18	C14 FP	D1 TN	15
	Total	115	4	119	94	3	97

Sensitivity=99/99+16* 100 = 99/115*100= 86.08%
Specificity = 2/2+2* 100 = 2/4*100= 50%
Positive prognostic value = 99/99+2* 100 = 99/101*100= 98%
Negative prognostic value = 2/2+16* 100 =2/18*100= 11.11%
Diagnostic Accuracy = 99+2/119 * 100 = 101/119* 100=84.87%

Table 8: CRP Vs Histopathology W.R.T Duration Of Symptoms (<2 days and >2 days)

		Histopathology					
		< 2 days			> 2 days		
		+	-	Total	+	-	Total
CRP	+	A136 TP	B2 FN	138	A45 TP	B1 FN	46
	-	C21 FP	D3 TN	24	C7 FP	D1 TN	8
	Total	157	5	162	52	2	54

Sensitivity=136/136+21*100 = 136/157*100= 86.62%
Specificity = 3/3+2*100 = 3/5*100= 60%
Positive prognostic value = 136/136+2*100 = 136/138*100= 98.55%
Negative prognostic value = 3/3+21*100 =3/24*100= 12.5%
Diagnostic Accuracy = 136+3/162 *100 = 139/162* 100=85.80%

Table 9: CRP Vs Histopathology WRT Socioeconomic Status (Poor, Middle and Rich)

		Histopathology								
		Poor			Middle			Rich		
		+	-	Total	+	-	Total	+	-	Total
CRP	+	A83 TP	B1 FN	84	A7 TP	B1 FN	77	A22 TP	B0 FN	22
	-	C13 FP	D2 TN	15	C12 FP	D2 TN	14	C3 FP	D1 TN	4
	Total	96	3	99	88	3	91	25	1	26

Sensitivity=83/83+13*100 = 83/96* 100= 86.45%
Specificity = 2/2+1*100 = 2/3* 100= 66.66%
Positive prognostic value = 83/83+1* 100 = 83/84*100= 98.80%
Negative prognostic value = 2/2+13* 100 =2/15*100= 13.33%
Diagnostic Accurateness = 83+2/99 * 100 = 85/99* 100=85.85%

Table 10: CRP Vs Histopathology WRT Obesity vs Non=Obesity

		Histopathology					
		Obese			Non-Obese		
		+	-	Total	+	-	Total
CRP	+	A41 TP	B0 FN	41	A141 TP	B2 FN	143
	-	C6 FP	D1 TN	7	C22 FP	D3 TN	25
	Total	47	1	48	163	5	168

Sensitivity=41/41+6*100 = 41/47*100= 87.23%
Specificity = 1/1+0*100 = 1/1*100= 100%
Positive prognostic value = 41/41+0*100 = 41/41*100= 100%
Negative prognostic value = 1/1+6*100 =1/7*100= 14.28%
Diagnostic Accuracy = 41+1/48 *100 = 42/48* 100=87.5%

Table 11: CRP Vs Histopathology WRT Diabetes Mellitus

		Histopathology					
		Diabetic			Non-Diabetic		
		+	-	Total	+	-	Total
CRP	+	A33 TP	B0 FN	33	A148 TP	B2 FN	150
	-	C5 FP	D1 TN	6	C24 FP	D3 TN	27
	Total	38	1	39	172	5	177

Sensitivity=33/33+5*100 = 33/38*100= 86.84%
Specificity = 1/1+0*100 = 1/1*100= 100%
Positive prognostic value = 33/33+0*100 = 33/33*100= 100%
Negative prognostic value = 1/1+5*100 =1/6*100= 16.66%
Diagnostic Accuracy = 33+1/39 *100 = 34/39* 100=87.17%

Table 12: CRP Vs Histopathology WRT Hypertensive and Non-Hypertensive

		Histopathology					
		Hypertensive			Non-Hypertensive		
		+	-	Total	+	-	Total
CRP	+	A27 TP	B 0 FN	27	A154 TP	B2 FN	156
	-	C 4 FP	D 1 TN	5	C24 FP	D4 TN	28
	Total	31	1	32	178	6	184

Sensitivity=27/27+4*100 = 27/31*100= 87.09%
Specificity = 1/1+0*100 = 1/1*100= 100%
Positive prognostic value = 27/27+0*100 = 27/27*100= 100%
Negative prognostic value = 1/1+4*100 =1/5*100= 20%
Diagnostic Accuracy = 27+1/32 *100 = 28/32* 100=87.5%

DISCUSSION

Acute appendicitis (AA) is the most common surgical condition requiring emergency surgery worldwide[19]. According to Global burden of disease 2013, AA is the most common diagnosis in patients seeking medical help in the emergency room due to acute abdomen causing 72,000 deaths among 16 million cases reported globally[11]. The lifetime risk of AA is 16.33% for males and 16.34% for females in South Korea[20]. According to Paduszyńska K et al. l, AA was the most common diagnosis in patients undergoing emergency surgery due to acute abdomen[21]. In Pakistan, about 400,000 appendectomies are routinely carried out in surgical departments each year[22].

Our study shows that mean SD ± 12.311 forty-eight years with. 55% of patients were male patients, and female patients were 45% were. Diagnostic precision of acute appendicitis CRP taking histopathology as well standard was examined as the sensitivity was 85.71%, specificity was 33.33%, Positive predictive value was 97.25%, 184.25% was Negative prognostic value, and the complete analysis accuracy was 84.25%. Comparable consequences were detected in another analysis by Xharra et al[23]. in which 173 patients surgically treated for AA showed that the severity of inflammation is directly related to increased levels of CRP with a diagnostic accuracy of 83.2%, a sensitivity of 85.1%, specificity72% and Positive predictive value of 94.7%[23].

In Streptococcus pneumonia-infected patients, CRP was elevated firstly [24]. Compared to other acute phase proteins, CRP levels also increase in tissue injuries, such as malignancies, rheumatic disease, and myocardial infarction[25]. As an acute phase protein, CRP level is elevated with the onset of the disease at eight hours, and its high levels are reached within twenty-four to forty-eight hours after the CRP level declines[26,27]. In the present study, all the included patients were diagnosed with histologically acute appendicitis based on C-reactive protein. The white blood cell count analyzed through SPSS and P valve was (P<0.001 and P=0.0025, respectively). 19.2% (n=15) negative explorations for acute appendicitis[28]. According to the literature of previous study have analyzed that, there is no increase in white blood cell counts

and CRP levels in the pre-operative who surgically removed the appendix[29].

CONCLUSION

The CRP test has a medium level of accuracy in identifying acute appendicitis. Despite the fact that this study had certain limitations, such as a small sample size for appendicitis-free patients.

As a result, the diagnosis of acute appendicitis should be based solely on clinical symptoms. Negative appendectomy may be avoided if individuals with normal test results are assessed with extra caution, even if the diagnostic utility of individual tests in acute appendicitis is constrained because to their low specificity. Before having an emergency appendectomy, these individuals may benefit from clinical surveillance and reassessment. Even when all tests are normal, acute appendicitis cannot be fully ruled out. Further diagnostic imaging tests are strongly advised if such individuals do not improve after a period of observation.

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