



ISSN NO. 2320-5407

Journal homepage: <http://www.journalijar.com>

INTERNATIONAL JOURNAL
OF ADVANCED RESEARCH

RESEARCH ARTICLE

Is There a Relationship Between Histopathological Features of Acute Appendicitis and Preoperative Acute Inflammatory Markers?

Sarmad Raheem Kareem

Department of Medical Microbiology, Koya University
Daniel Mitterrand Boulevard, Koya KOY45 AB64, Kurdistan Region – Iraq

Kahlan Raheem Karim

North West London Deanery
The Royal National Orthopedic Hospital/ Stanmore, London- UK

Manuscript Info

Manuscript History:

Received: 14 February 2014
Final Accepted: 12 March 2014
Published Online: April 2014

Key words:

appendicitis, histopathologic,
inflammatory markers, neutrophils

*Corresponding Author

Sarmad Raheem

Abstract

Acute appendicitis is a common surgical emergency, mainly clinically diagnosed with adjuvant laboratory tests, but a histopathologic study is the gold standards for diagnosis. A prospective study of fifty five cases of clinically diagnosed and surgically treated acute appendicitis investigated for preoperative acute inflammatory markers; total white blood cell count(WBC), neutrophils percentage, and C-reactive protein(CRP) to assess the accuracy of the laboratory tests and relationship with severity of pathological changes.

CRP and neutrophils percentage were found to be significantly (p value <0.05) associated with the severity of pathological changes as compared to normal appendectomies unlike total WBC count that showed no significant difference among pathologically normal and abnormal cases. *Copy Right, IJAR, 2014., All rights reserved*

Introduction

Acute appendicitis is the most common disease of surgical field worldwide and affects about 7% of the population. (Albayrak et al, 2011).

Despite some persisting controversy, there is a wide belief that most cases of acute appendicitis develop as a result of obstruction (Akbulut et al, 2011) and the most common cause of obstruction is a fecalith, but it may be a foreign body, a calculus, a gallstone, a tumor of the cecum, or a primary tumor of the appendix (Rosai, 2011). In children and young adults, diffuse lymphoid hyperplasia is another cause of obstruction (Luckmann et al, 1991).

Surgeons have many challenges about diagnosis, which is made primarily on the basis of the history and the physical examination (Alamgir et al, 2009), with additional assistance from laboratory and radiographic findings. (Lally et al, 2004).

It has indeed been suggested that measuring both white blood cell (WBC) count and C-reactive protein(CRP) could avoid up to one quarter of negative appendectomies in adult patients (Stefanutti et al, 2007).

White blood cell count or CRP values alone do not appear to provide any useful additional information to the surgeon. However, the sensitivity of the two combined tests is extremely high, and normal values of both WBC and CRP are very unlikely in pathologically confirmed appendicitis(Stefanutti et al, 2007) , but there considerable overlap with other inflammatory conditions mimicking acute appendicitis accounts for the low specificity and positive predictive value of these tests(Dalal et al, 2005).

Despite the introduction of sonography and computed tomography, the accuracy of diagnosis has improved only marginally in recent years (Gronroos, 2001), highlighting the need for better diagnostic tools. Although clinical history and examination are highly suggestive for acute appendicitis, the need for surgery can be excluded if both

WBC and CRP are within normal reference values (Yang et al, 2005). However histopathologic studies are the gold standards for diagnosis of acute appendicitis (Rosai, 2011).

Material and methods

Prospective study of fifty five cases clinically diagnosed as acute appendicitis and appendicectomy were done. Preoperative laboratory tests (C-reactive protein (CRP), total white blood cell (WBC) count and neutrophils percentage, and all tissue specimens had been formalin-fixed, paraffin- embedded and stained by Hematoxylin and Eosin (H and E) and examined by specialized pathologist. Cases were divided into 6 groups according to their pathological appearance (Rosai 2011):

1. Acute focal appendicitis with acute mucosal and submucosal inflammation.
2. Acute suppurative appendicitis.
3. Lymphoid hyperplasia.
4. Normal appendix without any pathologic changed.
5. Gangrenous appendicitis.
6. Perforative appendicitis.

SPSS-15 software was used to analyze data. Spearman's correlation coefficient was used to reveal the degree of linear correlation between staging of appendicitis study parameters.

For each of proportion confidence interval was calculated and in the all tests $P < 0.05$ is considered significant.

Results

Fifty five cases diagnosed preoperatively as acute appendicitis and appendicectomy was done, 27male cases (49 %) and 28 females cases (51 %). There was no significant sex difference in CRP, WBC count and neutrophil percentage.

The ages ranged from 6 to 65 years with a mean (26.3 ± 13.1) years, and majority of cases (29.1%) fall in the age group (18-27) years .Figure 1.

The incidence of pathologically normal appendicectomy was 3 cases (5.5%). The most frequent pathological change was acute suppurative appendicitis (36 cases) (65.5%).Figure 2.

The mean WBC count was (8654.54 ± 1588.74)cells/mm³ and the count higher seen in gangrenous group (10400 ± 1649.16), however it showed no significant difference among pathological groups.

C-reactive protein (CRP) and neutrophil percentage was higher in both gangrenous and perforative groups , where CRP showed significant relationship(p value <0.05) with different pathological changes of appendicitis except normal and acute focal appendicitis while neutrophil percentage was significantly different(p value <0.05) from pathologically normal and abnormal appendicectomy. Tables 1,2,3, and 4.

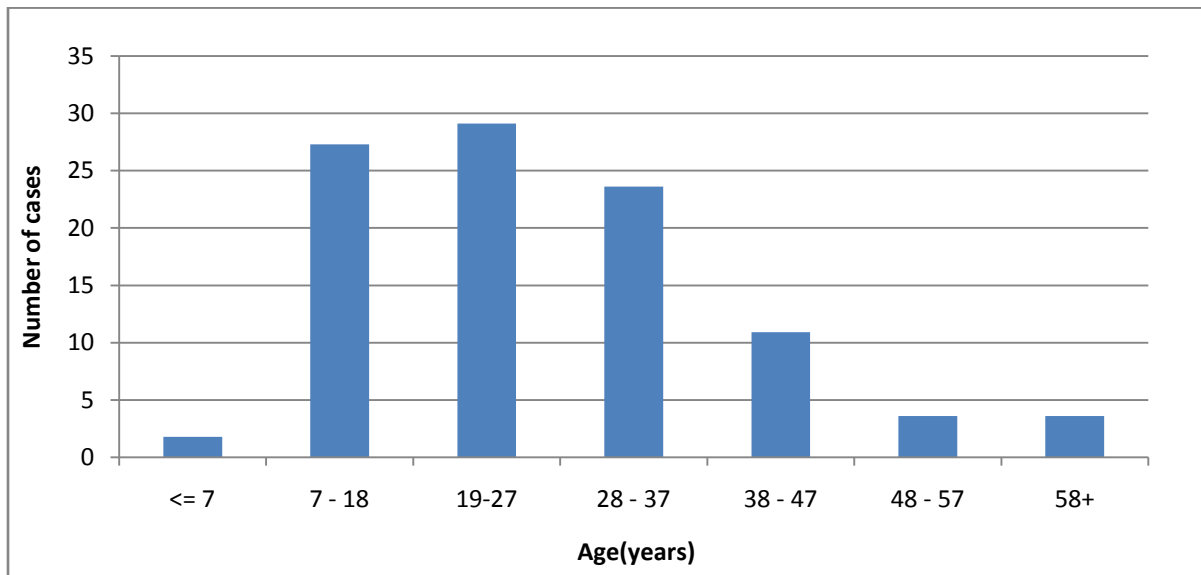


Fig 1: Age groups of 55 cases surgically treated as an acute appendicitis.

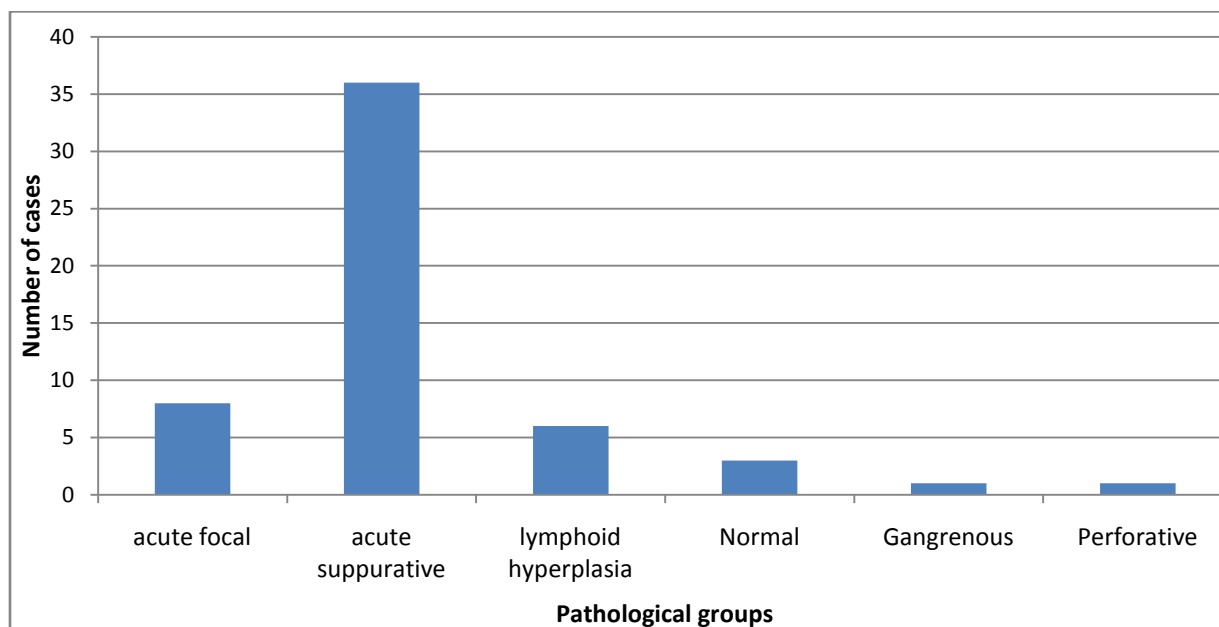


Fig 2: The frequency of pathological changes among appendicectomies.

Table 1: The mean value of total white blood cell count, C- reactive protein, and neutrophil percentage in different pathological groups.

Variable	Pathology	Mean± Std. Error
WBC Cells/mm ³	Acute focal	8830.000±679.968
	Acute suppurative	8306.095± 328.505
	Lymphoid hyperplasia	9505.556± 744.327
	Normal	9700.000± 1009.903
	Gangrenous	10400.000±1649.165
	Perforative	8950.000±1649.165
CRP mg/L	Acute focal	34.200± 14.810
	Acute suppurative	52.494± 7.155
	Lymphoid hyperplasia	10.667± 16.211
	Normal	60.000± 21.996
	Gangrenous	96.000± 35.919
	Perforative	96.000± 35.919
Neutrophils (%)	Acute focal	68.950± 2.341
	Acute suppurative	68.876± 1.131
	Lymphoid hyperplasia	61.389± 2.563
	Normal	67.500± 3.478
	Gangrenous	76.000± 5.679

Perforative	80.000± 5.679
--------------------	----------------------

Table 2: Total white blood cell count (cells/mm³) difference in pathological groups within 95% confidence interval for difference.

Variable	(I) Pathology	(J) Pathology	Mean Difference (I-J)	Std. Error	P value*
WBC (Cell/mm ³)	Acute focal	Acute suppurative	523.905	755.164	0.493
		Lymphoid hyperplasia	-675.556	1008.156	0.507
		Normal	-870.000	1217.481	0.480
		Gangrenous	-1570.000	1783.844	0.385
		Perforative	-120.000	1783.844	0.947
	Acute suppurative	Acute focal	-523.905	755.164	0.493
		Lymphoid hyperplasia	-1199.460	813.595	0.150
		Normal	-1393.905	1061.989	0.198
		Gangrenous	-2093.905	1681.565	0.222
		Perforative	-643.905	1681.565	0.704
	Lymphoid hyperplasia	Acute focal	675.556	1008.156	0.507
		Acute suppurative	1199.460	813.595	0.150
		Normal	-194.444	1254.562	0.878
		Gangrenous	-894.444	1809.355	0.624
		Perforative	555.556	1809.355	0.761
	Normal	Acute focal	870.000	1217.481	0.480
		Acute suppurative	1393.905	1061.989	0.198
		Lymphoid hyperplasia	194.444	1254.562	0.878
		Gangrenous	-700.000	1933.817	0.720
		Perforative	750.000	1933.817	0.701
	Gangrenous	Acute focal	1570.000	1783.844	0.385
		Acute suppurative	2093.905	1681.565	0.222
		Lymphoid hyperplasia	894.444	1809.355	0.624
		Normal	700.000	1933.817	0.720
		Perforative	1450.000	2332.271	0.538
	Perforative	Acute focal	120.000	1783.844	0.947
		Acute suppurative	643.905	1681.565	0.704
		Lymphoid hyperplasia	-555.556	1809.355	0.761
Normal		-750.000	1933.817	0.701	
Gangrenous		-1450.000	2332.271	0.538	

Table 3: C- reactive protein (mg/L) difference in pathological groups within 95% confidence interval for difference.

Variable	(I) Pathology	(J) Pathology	Mean Difference (I-J)	Std. Error	P value*
CRP (mg/L)	Acute focal	Acute suppurative	-18.294	16.448	0.274
		Lymphoid hyperplasia	23.533	21.958	0.292
		Normal	-25.800	26.517	0.338
		Gangrenous	-61.800	38.852	0.121
		Perforative	-61.800	38.852	0.121
	Acute suppurative	Acute focal	18.294	16.448	0.274
		Lymphoid hyperplasia	41.828	17.720	0.024
		Normal	-7.506	23.130	0.748
		Gangrenous	-43.506	36.625	0.243
		Perforative	-43.506	36.625	0.243
	Lymphoid hyperplasia	Acute focal	-23.533	21.958	0.292
		Acute suppurative	-41.828	17.720	0.024
		Normal	-49.333	27.324	0.080
		Gangrenous	-85.333	39.408	0.038
		Perforative	-85.333	39.408	0.038
	Normal	Acute focal	25.800	26.517	0.338
		Acute suppurative	7.506	23.130	0.748
		Lymphoid hyperplasia	49.333	27.324	0.080
		Gangrenous	-36.000	42.119	0.399
		Perforative	-36.000	42.119	0.399
	Gangrenous	Acute focal	61.800	38.852	0.121
		Acute suppurative	43.506	36.625	0.243
		Lymphoid hyperplasia	85.333	39.408	0.038
		Normal	36.000	42.119	0.399
		Perforative	4.65E-013	50.797	1.000
	Perforative	Acute focal	61.800	38.852	0.121
		Acute suppurative	43.506	36.625	0.243
		Lymphoid hyperplasia	85.333	39.408	0.038
Normal		36.000	42.119	0.399	
Gangrenous		-4.65E-013	50.797	1.000	

*P value less than 0.05 is significant.

Table 4: Neutrophil percentage difference in pathological groups within 95% confidence interval for difference.

Variable	(I) Pathology	(J) Pathology	Mean Difference (I-J)	Std. Error	P value*
	Acute focal	Acute suppurative	0.074	2.600	0.977
		Lymphoid hyperplasia	7.561	3.472	0.037
		Normal	1.450	4.192	0.732
		Gangrenous	-7.050	6.143	0.259

Neutrophil (%)	Acute suppurative	Perforative	-11.050	6.143	0.081
		Acute focal	-0.074	2.600	0.977
		Lymphoid hyperplasia	7.487	2.802	0.012
		Normal	1.376	3.657	0.709
		Gangrenous	-7.124	5.790	0.227
	Lymphoid hyperplasia	Perforative	-11.124	5.790	0.063
		Acute focal	-7.561	3.472	0.037
		Acute suppurative	-7.487	2.802	0.012
		Normal	-6.111	4.320	0.167
		Gangrenous	-14.611	6.231	0.025
	Normal	Perforative	-18.611	6.231	0.005
		Acute focal	-1.450	4.192	0.732
		Acute suppurative	-1.376	3.657	0.709
		Lymphoid hyperplasia	6.111	4.320	0.167
		Gangrenous	-8.500	6.659	0.211
	Gangrenous	Perforative	-12.500	6.659	0.069
		Acute focal	7.050	6.143	0.259
		Acute suppurative	7.124	5.790	0.227
		Lymphoid hyperplasia	14.611	6.231	0.025
		Normal	8.500	6.659	0.211
Perforative	Perforative	-4.000	8.031	0.622	
	Acute focal	11.050	6.143	0.081	
	Acute suppurative	11.124	5.790	0.063	
	Lymphoid hyperplasia	18.611	6.231	0.005	
	Normal	12.500	6.659	0.069	
	Gangrenous	4.000	8.031	0.622	

*P value less than 0.05 is significant.

Discussion

Acute appendicitis is characterized by the development of inflammation at a local level, followed by a more generalized inflammatory response. The rationale of laboratory tests in the diagnosis of acute appendicitis is based on the possibility of detecting signs of systemic inflammation with a diagnostic tool that is widely available and easy to perform, is minimally invasive, has limited costs, and can be repeated if necessary (Wilcox et al,1997).

The peak incidence in the age groups was (7-18) and a (19-27) year which is usually roughly parallels that of lymphoid development, with peak incidence in the late teens and twenties. (Akbulut et al, 2011).

The rate of negative appendectomy was 5.4 % which is better than the record in other studies (11.83%) (Seetahal et al, 2011).

This study showed no significant change in WBC count in different pathological groups which is comparable to the study that showed that the WBC count is nonspecific for appendicitis as elevations are noted in nearly half of all patients with gastroenteritis, mesenteric adenitis, pelvic inflammatory disease, and other infectious disorders (Rothrock et al 2000) limited studies suggest that CRP may be more sensitive (>90%) than the WBC count in detecting appendiceal perforation and abscess formation, conditions more common in children.(Peitola et al, 1986)(

Sanchez et al, 1998). Sequential CRP measurements may be more sensitive than a single measurement, but the specificity did not improve or decline during sequential testing. (Eriksson et al, 1994).

Inflammatory markers such as WBC and CRP are poorly reliable in confirming the presence of an acute appendicitis because of their low specificity in adults as well as in children (yang et al 2005).

On the other hand CRP showed significantly different elevation in pathological groups as compared to normal and acute focal appendicitis indicating that it is less useful in early cases of appendicitis but its value is increased with more severe pathological changes (Table3) although this may be different from other studies since we used 6.0 mg/L as the upper reference value for CRP as opposed to 10.0 as reported by others (Lycopoulou et al, 2005).

Neutrophil percentage was a better inflammatory marker for predicting the severity of acute appendicitis as it showed significant increase in pathologically confirmed appendicitis as compared with negative appendectomy making it a better diagnostic tool.

Conclusion

Preoperative C-reactive protein and neutrophil percentage are useful markers to predict the severity of pathological changes of acute appendicitis requiring earlier surgical treatment and avoid unnecessary complications.

References

- Akbulut,S., Tas,M., Sogutcu,N., Arikanoglu,Z., Basbug,M., Ulku,A., Semur,H., Yagmur,Y., (2011).Unusual histopathological findings in appendectomy specimens: A retrospective analysis and literature review .World J. Gastroenterol. , 17(15): 1961-1970.
- Alamgir, Munir,A., Qadir,S.,(2009):Acute appendicitis : Role of alverado scoring system in the diagnosis .Gomal Journal of Medical Sciences ,7(2):89-91.
- Albayrak,Y., Albayrak,A., Celik,M., Gelincik,I., Demiryilmaz,I., Yildirim,R., and Ozogul,B.(2011):High mobility group box protein-1 (HMGB-1) as a new diagnostic marker in patients with acute appendicitis. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine, 19:27.
- Dalal, I., Somekh, E., Bilker-Reich, A., Boaz, M.,Gorenstein, A.,Serour, F.(2005): Serum and peritoneal inflammatory mediators in children with suspected acute appendicitis. Arch. Surg., 140:169- 73.
- Eriksson, S., Granstrom, L., Carlstrom, A. (1994): The diagnostic value of repetitive preoperative analyses of C-reactive protein and total leucocyte count in patients with suspected appendicitis. Scand. J. Gastroenterol., 29:1145-1149.
- Gronroos JM. (2001): Do normal leukocyte count and C-reactive protein value exclude acute appendicitis in children? Acta. Paediatr. , 90: 649- 51.
- Lally, K.P., C.S. Cox and R.J. Andrassy. (2004): Appendix, In: Townsend, C.M., R.D. Beauchamp, B.M. Evers and K.L. Mattox, Sabiston textbook of surgery, 17th Ed., Elsevier Sunders Co., Philadelphia, pp: 1381-1400.
- Luckmann, R., Davis, P. (1991): The epidemiology of acute appendicitis in California, Racial, gender, and seasonal variation. Epidemiology, 2:323-330.
- Lycopoulou, L., Mamoulakis, C., Hantzi, E.,Demetriadis,D,Antypas, S.,Giamaki,M.(2005): Serum amyloid A protein levels as a possible aid in the diagnosis of acute appendicitis in children. Clin. Chem. Lab. Med, 43:49- 53.
- Rosai, J. (2011): Rosai and Ackerman Surgical Pathology, 9th Ed., Mosby Co., China, pp: 757-61.
- Rothrock, S., Pagane,J.(2000): Acute Appendicitis in Children: Emergency Department Diagnosis and Management. Annals of Emergency Medicine, 36:1.
- Sanchez, EJ., Luis, GM., Vazquez, R.(1998): Diagnostic value of C-reactive protein in suspected appendicitis in children. An. Esp. Pediatr., 48:470-474.
- Seethahal, SA., Bolorunduro, OB, Sookdeo, TC., Oyetunji, TA., Greene, WR., Frederick, W., Cornwell, EE 3rd., Chang, DC., Siram ,SM.(2011): Negative appendectomy: a 10-year review of a nationally representative sample. Am. J. Surg., 201(4):433-7.
- Stefanutti G., Ghirardo, V., Gamba, P.(2007): .Inflammatory markers for acute appendicitis in children: are they helpful? Journal of Pediatric Surgery, 42, 773–776.
- Wilcox, RT., Traverso, LW. (1997): Have the evaluation and treatment of acute appendicitis changed with new technology? Surg. Clin. North Am., 77:1355- 70.
- Yang, HR., Wang, YC. Chung, PK., Chen, WK., Jeng, LB., Chen, RJ. (2005): Role of leukocyte count, neutrophil percentage, and C-reactive protein in the diagnosis of acute appendicitis in the elderly. Am. Surg., 71:344 - 7.