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Original Research Article

Role of C Reactive Protein, White Blood Cell Counts, Polymorph Percentage and Histopathological Findings in Diagnosing Appendicitis

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Abstract

Background*:* Acute appendicitis is the most common surgical emergency associated with an acute phase reaction. The diagnosis of the same is based on detailed clinical history and examination, laboratory and imaging interventions. The aim of the study is to study the role of C- reactive protein, white blood cell counts and polymorph percentage with histopathological examination for accurate diagnosis of appendicitis.

Materials and Methods*:* It's a retrospective study conducted in, patients presenting with features suggestive of appendicitis and were taken from1st January 2017 to 31st July 2017. The various clinical manifestations were considered and total of 100 cases were included in the study. The correlation of clinical presentation, with laboratory markers like CRP, total WBC counts and Neutrophil percentage with histopathological presentation was done.

Results*:* The CRP levels significantly differed from gangrenous appendicitis (Group C) and catarrhalis and phlegmonous appendicitis (Group B). As compared to Total leucocyte counts and polymorphs percentage the CRP assay had sensitivity of 100% and specificity of 90% in comparison to WBC counts and Polymorph percentages which had a sensitivity of 55% and 75%. The total diagnostic accuracy of CRP assay was 97.7%

Conclusion*:* The diagnostic accuracy of C reactive protein is not significantly higher than WBC and Neutrophil percentages. Though the values of CRP are directly proportional to the severity of inflammation. The combination of CRP, WBC and the polymorph counts together have a greater diagnostic accuracy in cases of appendicitis.

Keywords: Acute Appendicitis; CRP; WBC; Neutrophil Percentage; Histopathology.

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Introduction

Acute appendicitis is the most common abdominal surgical emergency with an estimated lifetime prevalence of 7% and is the most common source of community acquired intra-abdominal infections [1,2,3]. The clinical presentation is often variable and atypical and the diagnosis is difficult because the symptoms overlap with other conditions [4]. The diagnosis is chiefly made depending upon the presenting history, clinical evaluation and physical examination [5]. It is further aided by laboratory investigations such as white blood cell counts, differential counts specially neutrophil count, C reactive protein and other non-interventional methods like ultrasonography and CT scan. The fundamental clinical decision in the diagnosis of a patient with suspected appendicitis is whether to operate or not. More idealistically the goal is to treat all cases of appendicitis without surgical intervention. In cases with presentation of catarrhalis (inflammation within the mucous

membrane) or phlegmonous (inflammation in all three layers) appendicitis, immediate management with non-surgical techniques have proven beneficial, safe and effective [6]. A prospective multi-center study randomized control trial proved that acute non perforated appendicitis can be treated successfully with antibiotics [7].

In clinical set up diagnosing appendicitis on basis of surgical indicators is difficult. An estimate has stated that accuracy of clinical diagnosis of acute appendicitis is between 76% and 92%, accurate diagnosis of the same is still difficult resulting in high perforation rates and negative appendicectomies [10]. The advent of ultrasonography in the last two decades and computed tomography in the last decade has remarkably changes the scenario of negative appendectomies but perforations still remain high (22-62%) [11]. Also heavy reliance on these imaging modalities have certain disadvantages like exposure to radiation with CT may increase a lifetime risk of cancer and technical assistance is needed for equipment use and interpretation of results which might not be available universally in all hospitals. Widely available laboratory tests such as white blood cell counts, neutrophil percentage and serum level of CRP have been important diagnostic aids [8]. Some reports have indicated that appendicitis is unlikely when the white blood cell counts and CRP values are normal [9]. White blood cell count alone is neither sensitive nor specifically diagnostic of acute appendicitis and is increased in 70% of patients with other causes of pain in right lower abdominal quadrant. C reactive protein is more specific that WBC but is less sensitive in early acute appendicitis. CRP is more sensitive in detecting appendiceal perforation and abscess formation. In view of the low positive predictive value of traditional inflammatory markers, studies have proven that combined use of WBC and CRP may enhance the negative predictive value [12].

CRP is a nonspecific inflammatory marker used routinely in diagnosing acute abdomen. It was discovered in 1930 and was so named because it reacted with the pneumococcal C polysaccharide in the plasma of patients during acute phase of pneumococcal pneumonia [13]. An acute phase protein which is produced in the liver. Its normal concentration in plasma is less than 10mg/l but within 8-12 hrs. of infection or trauma it shows a remarkable increase, hence being an important diagnostic tool in clinical practice. Production of CRP is controlled by interleukin 6and in a few minute's increases from 10 to 1000 times. Many reports have investigated the significance of raised CRP measurements in improving the diagnostic accuracy of acute appendicitis [8,9,10].

The aim of this study was to analyze the role of CRP values in accurate diagnosis of appendicitis with White blood cell counts, Neutrophil percentage, clinical diagnosis and histopathological correlation.

Methods

All the patients presenting with features suggestive of appendicitis were taken from January 1 2017 to 31 July 2017 at D Y Patil Medical college and Research Centre Pimpri, Pune. Clinical signs of acute appendicitis as determined by the surgeon were considered and the duration of the presentation were documented at the time of admission. The signs considered were tenderness at the right lower quadrant, percussion and rebound tenderness, localized guarding and diffusely rigid abdomen. A total of 100 cases were included in the study amongst which there were 34 females and 66 males and the age ranged from14-66 yrs. All the cases had clinical signs of appendicitis, and underwent open appendectomy. Venous samples were taken when the patients had presented to ward for white blood cell counts, neutrophil percentage and C reactive protein levels.White blood counts and differential polymorph counts were measured by the hematology analyzer (Benesphera 5- part hematology analyzer). The normal WBC counts value in our laboratory are 4000 to 10000/cumm and levels above 10000/cumm were considered above normal. The polymorphs were considered high if they were >75%. The CRP values were evaluated by CRP turbilatex Reactivos GPL reagent method.The removed appendix was fixed in 4% formalin and stained with hematoxylin and eosin (H&E) and were examined by pathologists. The cases were identified into three groups according to ShastariM H S, 2006: Group A normal appendix; Group B catarrhalis appendicitis (inflammation within the mucous membrane) and phlegmonous appendicitis(with inflammation in all three layers) and Group C included gangrenous or perforated appendix [14]. Final diagnoses was based on histopathological examination and in case of perforation on macroscopic conclusions of the surgeon.

Statistical Analysis

All variables were further analyzed for significant differences. The receiver-operating characteristics (ROC) curves were drawn to define optimum sensitivity, specificity, cut off values, predictive values and diagnostic accuracy, determined by area under the curve (AUC) of the studied laboratory markers.

Results

Out of the total 100 cases, 66 males and 34 females were recorded with a M: F ratio of 1.9:1. The age ranges were from 14 yrs. to 66 yrs. with average of 31.6 yrs. and SD (11.52yrs) (Table 1).

According to histopathology reports Group A comprised of normal appendicitis comprising of 20% of

cases, followed by Group B comprising 62% of cases which included catarrhal and phlegmonous appendicitis and Group C comprised of gangrenous appendicitis having 18% of cases (Table 2).

The study of other laboratory parameters was also done and tabulated. Although they were done in all the cases two cases did not have CRP measures and so they were excluded from the study. The CRP values ranged from 5 mg/L to 178mg/L with SD of 40.6mg/L. The total leukocyte count varied from 4,600 to 29,800/ml and the mean recorded was 12,978 with SD of 5558.76. The polymorph count ranged from 51%to 88 % with SD of 9.1%. (Table 3)

All the cases were divided into three groups as Group A comprising of normal appendix or negative appendectomy, group B comprising of Catarrhal & Phlegmonous appendix and group C comprising of necrotic and gangrenous appendicitis. Common clinical presentations associated with negative appendectomy included nonspecific abdominal pain, ruptured ovarian cyst, mesenteric lymphadenitis and urinary infections. The CRP values in group A ranged from 5.2 to 11.1 mg/L with a mean of 10.81 mg/L. In group B the values of CRP ranged from 16.0 to 68.9 mg/L with a mean of 39.6 mg/L and in group C the CRP ranged from 69.0 to 178.3 mg/L with mean of 115.2 mg/L. Total cases were 98 amongst which true positive cases were 78% and false positive were 02%. False negative rate recorded in the study was 18%. On the basis of clinical signs and symptoms the diagnosis was true in 87.3% of cases and false in 12.7% cases. In the present study the positive predictive value of CRP was 97.5%, specificity 90%, sensitivity 100% and diagnostic accuracy of 97.96%.

Similarly, the WBC counts polymorphs percentage were assessed. Group A had a total of 20% of cases. The WBC counts ranged from 7,400 to 12,800/cu mm. Group B had 62% cases with total count ranging from 4,600 to 21,000/ cumm. The third group C had a total of 18 cases with total counts ranging from15,100 to 29,800 /cu mm. The total true positive recorded were 44%, true negative cases were 20%and false positive were36%. Sensitivity of 55%, specificity 100%, positive predictive value 100% and negative predictive value was35.71%. Total accuracy of 64% was recorded. Differential count of polymorphs recorded were highest for group B that was 62% ranging from59 to 78%, this was followed by group A with total cases recorded were 20% and the range was 54 to 76%, lastly the least number of cases recorded were in Group C i.e. 18% but showed highest differential range 73 to 81%. A specificity of 40% was recorded and sensitivity of 75% was seen. Positive predictive value was 83.33% and a negative predictive value of 28.57%. Total diagnostic accuracy noted was 68%.

The WBC and CRP levels were elevated in 48 cases of (48.9%) with positive histopathological findings in Group B and C. In these groups 30 patients had normal TLC count and two cases had presented with normal CRP values. A total of 80 patients in this group had raised CRP values and 48 cases had increased total leukocyte count. In group A eight cases had presented with normal CRP values and 16 cases had normal total leukocyte count. Elevated CRP values were noted in ten cases of group A and increased leukocyte count was seen in four cases. In group A ten cases had normal polymorph counts while two had increased differential counts of neutrophils. In group B and C, 46 cases had normal count of polymorphs and 38

Table 1: Distribution of cases according to gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	F	34	34.0	34.0	34.0
	M	66	66.0	66.0	100.0
	Total	100	100.0	100.0	-

Table 2: Distribution on histopathological features of Appendicitis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal (Group A)	20	20.0	20.0	20.0
	Catarrhal & Phlegmonous (Group B)	62	62.0	62.0	82.0
	Gangrenous (Group C)	18	18.0	18.0	100.0
	Total	100	100.0	100.0	

Table 3: Descriptive Statistics of laboratory values

	N	Minimum	Maximum	Mean	Std. Deviation
CRP value (mg/L)	98	5	178	47.53	40.617
Age	100	14	66	31.06	11.525
TLC	100	4600	29800	12978.00	5558.769
Polymorphs	100	51	88	69.84	9.192
Valid N (list wise)	98				

cases had raised polymorph counts. Combining of all three parameters (WBC, CRP and percentage of polymorph count) raised, were noted in 3 patients in group A and two cases had one of the parameters raised. In group B and C, total of 43 patients had presented with significant values in all the three parameters. Sensitivity and specificity of all three parameters together have been depicted in the figure.

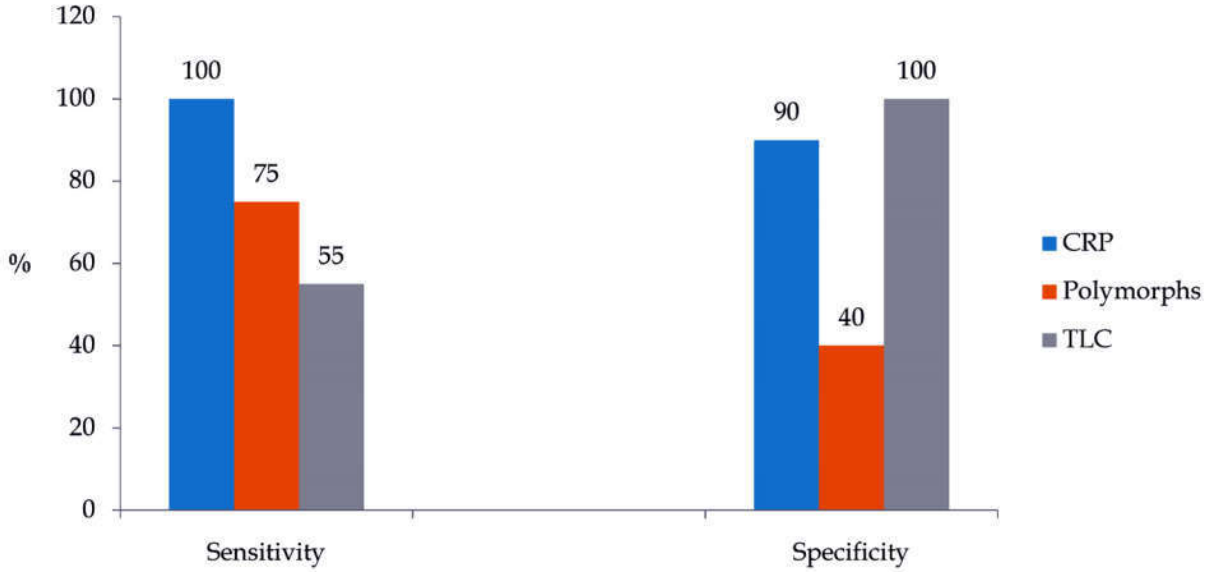

Fig. 1: Comparison of sensitivity and specificity of CRP, TLC and polymorphs

Fig. 2: ROC Curve

Case Processing Summary

Appendicitis	Valid N (list wise)
Positive[a]	78
Negative	20
Missing	2

Larger values of the test resultvariable(s) indicate stronger evidence for a positive actual state.
a. The positive actual state is Appendicitis.

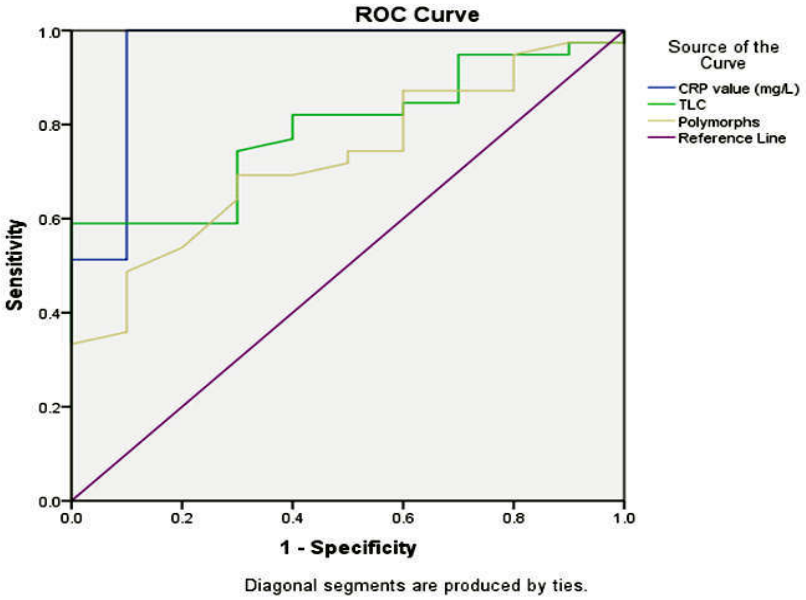

Fig. 3: Receiver operating characteristic curve (Diagonal line) for CRP, TLC, Polymorph counts.

Test Result Variable(s)	Area Under the Curve				
	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
CRP value (mg/L)	.951	.033	.000	.886	1.000
TLC	.788	.047	.000	.697	.880
Polymorphs	.727	.055	.002	.619	.835

The test result variable(s): TLC, Polymorphs has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.
a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

Test Result Variable(s)	Coordinates of the Curve		
	Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
CRP value (mg/L)	4.00	1.000	1.000
	5.50	1.000	.900
	6.50	1.000	.400
	8.00	1.000	.300
	10.00	1.000	.200
	13.50	1.000	.100
	17.50	.949	.100
	21.00	.923	.100
	23.50	.897	.100
	25.00	.872	.100
	26.50	.821	.100
	27.50	.744	.100
	30.50	.718	.100
	34.50	.692	.100
	36.50	.667	.100
	37.50	.641	.100
	38.50	.564	.100
	42.00	.513	.100
	45.50	.513	.000
	50.00	.436	.000
	55.00	.410	.000
	56.50	.385	.000
	59.00	.359	.000
	61.50	.333	.000
	64.00	.308	.000
	67.50	.256	.000
	83.00	.154	.000
	103.50	.128	.000
	118.50	.103	.000
	137.00	.077	.000
	158.50	.051	.000
	174.00	.026	.000
	179.00	.000	.000
TLC	4599.00	1.000	1.000
	5150.00	.974	1.000
	6250.00	.974	.900
TLC	6950.00	.949	.900
	7250.00	.949	.800
	7450.00	.949	.700
	7650.00	.897	.700
	7850.00	.872	.700
	7950.00	.846	.700
	8100.00	.846	.600
	8300.00	.821	.600
	8550.00	.821	.500

	8750.00	.821	.400
	8850.00	.769	.400
	9000.00	.744	.300
	9200.00	.692	.300
	9400.00	.667	.300
	9550.00	.641	.300
	9700.00	.590	.300
	10500.00	.590	.200
	12000.00	.590	.100
	12850.00	.590	.000
	13650.00	.564	.000
	14550.00	.538	.000
	14850.00	.513	.000
	15050.00	.487	.000
	15450.00	.462	.000
	16150.00	.436	.000
	16700.00	.385	.000
	16950.00	.333	.000
	17200.00	.308	.000
	17450.00	.282	.000
	17550.00	.256	.000
	17700.00	.231	.000
	17900.00	.205	.000
	18100.00	.179	.000
	18550.00	.154	.000
	19150.00	.128	.000
	20200.00	.103	.000
TLC	22900.00	.077	.000
	24900.00	.051	.000
	27400.00	.026	.000
	29801.00	.000	.000
Polymorphs	50.00	1.000	1.000
	52.00	.974	1.000
	53.50	.974	.900
	54.50	.949	.800
	55.50	.897	.800
	57.50	.872	.800
	59.50	.872	.600
	61.00	.846	.600
	62.50	.821	.600
	64.00	.744	.600
	65.50	.744	.500
	66.50	.718	.500
	67.50	.692	.400
	68.50	.692	.300
	69.50	.667	.300
	70.50	.641	.300
	71.50	.538	.200
	72.50	.487	.100
	74.00	.410	.100
	75.50	.359	.100
	76.50	.333	.000
	77.50	.256	.000
	78.50	.179	.000
	80.00	.103	.000
	82.50	.077	.000
	85.50	.051	.000
	87.50	.026	.000
	89.00	.000	.000

The test result variable(s): TLC, Polymorphs has at least one tie between the positive actual state group and the negative actual state group. a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Discussion

Appendicitis has invariably been treated by surgical intervention. However, non-surgical and conservative methods have also proven beneficial [6]. Traditional practice of interval appendectomy has been practiced for long in which patients who not have recurring episodes of appendicitis in 3 to 6 months may not need an appendectomy at all, but that leaves the clinician or surgeon with the question whether to go for surgical means or manage with antibiotics. The severity of appendicitis, determines the course of therapy. So parameters which can aid in the decision of the course of treatment were needed. Acute phase proteins are defined as one, whose plasma concentration increases or decreases by at least 25% during inflammatory disorders.The changes in the concentration of acute phase proteins are largely due to changes in their production by hepatocytes. The magnitude of the increase varies from 50% for ceruloplasmin and several other complements to as much as 1000 times in the case of C Reactive Proteins and serum amyloid A [15]. An aid to the clinical presentation, laboratory parameters like CRP, white blood cell counts and Neutrophil percentage would be useful in deciding whether treatment should be considered with surgery or antibiotic course. The aim of the current study is to analyze the role of CRP values in accurate diagnosis of appendicitis with White blood cell counts, Neutrophil percentage, clinical diagnosis and histopathological correlation. The study inferred that white blood cell counts and neutrophil count are not accurate indicators for surgery, however CRP was significantly high in catarrhalis and phlegmonous appendicitis but a remarkable increase was noted in the gangrenous appendicitis along with white blood cell counts and neutrophil percentages. The ROC curve indicated the optimal cut off was 6mg/dl. CRP level along with the clinical presentation of the patient should be taken into consideration before deciding the course of treatment.

In a study conducted by Mohammad et.al they concluded that positive CRPis more accurate than the WBC and neutrophil counts and combined together they have better diagnostic accuracy [16]. In a study conducted by Asfar et al, they reported a sensitivity and specificity of CRP as 86.6% and 93.6% respectively. They had concluded that a normal CRP value probably indicates a non-inflamed appendix and it is a more sensitive test than the WBC and neutrophil counts and the combination of both significantly increases sensitivity and specificity [17]. Study conducted by Erkassap concluded that sensitivity and specificity of CRP were 96% and 78% respectively and the positive predictive value was 100% [18]. In another study it was concluded combined usage of the WBC, neutrophil count and the CRP monitoring increased the positive predictive value [19].

In our study, the CRP values ranged from 5.2 to 11.1 mg/L in group A. In group B the values of CRP ranged from 16.0 to 68.9 mg/L with a mean of 39.6 mg/L and in group C the CRP ranged from 69.0 to 178.3 mg/L. The patients presenting with catarrhalis, phlegmonous and necrotic appendicitis presented with increased CRP values as compared to normal appendicitis. This parameter can be used as a surgical indicator although in aid of other clinical presentations and other investigatory findings. Numerous previous studies have indicated that CRP level enhances the precision of diagnosis of acute appendicitis, but not a critical surgical indicator. Another retrospective study has documented the sensitivity of CRP as greater than 90% [20]. A prospective study concluded it is important to measure serial CRP levels and white blood cell counts in patients with suspected appendicitis. The sensitivity of CRP levels in predicting appendicitis was 60% on admission and increased to 100% by fourth day in the sampled blood. In contrast white blood cell counts showed a sensitivity of 95% on admission but dropped to 75% on fourth day of sample collection [21].

WBC counts and polymorphs percentage were also assessed in our study. Group A with total 20% of cases had WBC counts ranging from 7,400 to 12,800/cu mm. Group B had 62% cases with total count ranging from 4,600 to 21,000/cu mm. The third group C had a total of 18 cases with counts ranging from15,100 to 29,800/cu mm. Differential count of polymorphs recorded were highest for group B that was 62% ranging from 59 to 78%, this was followed by group A with the range of 54 to 76%, lastly the least number of cases recorded were in Group C i.e. 18% but showed highest differential range 73 to 81%. Anderson in their prospective study concluded that the WBC and polymorph counts are better criteria for subsequent examinations [22].

The mean values of CRP in catarrhal and phlegmonous appendicitis was much higher as compared to normal appendix and was significantly high in gangrenous appendicitis. The WBC and neutrophil percentage are also increased in correlation with severity of inflammation. None of these are 100 % diagnostic. The CRP measurement or leukocyte counts are by itself not completely preventive for negative appendectomy. Ancillary investigative methods like CRP, Leukocyte counts and Polymorphs percentage with CT scan and Ultrasonography give a better perspective to diagnosis in cases of acute appendicitis.

Conclusion

The diagnostic accuracy of C reactive protein is not significantly higher than WBC and Neutrophil percentages. The values of CRP are directly proportional to the severity of inflammation. The combination of CRP, WBC and the polymorph counts together have a greater diagnostic

accuracy in cases of appendicitis. With the aid of these parameters, clinical presentation and combination of other ancillary techniques significant decrease in false positive and false negative cases have been made but none of these parameters alone are 100% diagnostic of appendicitis.

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References

1. Gwynn LK. The diagnosis of acute appendicitis: clinical assessment versus computed tomography evaluation. J Emerg. Med. 2001;21(2):119-123.
2. Pal k, Khan A. Appendicitis a continuing challenge. J Pak Med Assoc. 1998;48(7):189-92.
3. Sartelli M Et al. Complicated intra-abdominal infections in Europe: preliminary data from the first three months of the CIAO Study. World Journal of Emergency Surgery 2012,7(1):15.
4. Andersson RE. Meta- analysis of the clinical and laboratory diagnosis of appendicitis. Br. J Surg.2004;91(1):28-37.
5. Xharra Et al. Correlation of serum C-reactive protein, white blood count and neutrophil percentage with histopatology findings in acute appendicitis. World Journal of Emergency Surgery. 2012;7:27.
6. Oliak D, Yamini D, Udani VM, Lewis RJ, Arnell T, Vargas H, Stamos MJ: Initial non operative management for peri-appendiceal Abscess. Disease of Colon Rectum 2001,44:936-41.
7. Styrud J, Eriksson S, Nilsson I,AhibergG,Haapaniemi S, Neovius G, Rex L, Badume I, granstorm L. Appendicectomy versus antibiotic treatment in acute appendicitis. A prospective multicenter randomized controlled trial. World J Surg 2006,30:1033-37.
8. Yildiram O, Solak C, Kocer B, Unal B, Karabeyoglu M, Bozkurt B, Aksaray S, Cengiz O: The role of serum inflammatory markers in acute appendicitis and their success in preventing negative laparotomy. J Invest Surg 2006, 19:345-52.
9. Yang HR, Wang YC, Chung P K,Chen W K, Jeng LB, Chen RJ: Laboratory tests in patients with acute appendicitis. ANZ J Surg 2006;76:71-74.
10. ShakhatrehHS:The accuracy of C reactive protein in the diagnosisof acute appendicitiscomapred with that of clinical diagnosis. Med Arh 2000;54(2)109-110.
11. Khan MN,DavieE,Irshad K: The role of white cell count and Creactive Protein in the diagnosis of acute appendicitis. JAyub Med Coll Abbottabad 2004;16(3):17-19.
12. Andersson RE. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. Br J Surg 2004;91:28-37.
13. Tillett WS, Francis TJr Serological reactions in pneumonia with non-protein somatic fraction of pneumococcus. J Exp Med 1930;52:561-71.
14. Shashtari MHS, Aakarpour S, Alamshah M, Elahi A: Diagnostiv value of Quantitative CRP measurement in patients with acute appendicitis. Pak J Med Sci 2006 Jul-Sep;(3):300-303.
15. Morley J.J. Kushner I. Serum C reactive protein levels in Disease. Ann N Y Acad Sci 1982;389:406-18.
16. Mohammad AA, Daghman NA, Aboud SM, Oshibi HO. The diagnostic value of C reactive protein, white blood cell count and neutrophil percentage in childhood appendicitis. Saudi Med J 2004;25(9):1212-1215.
17. Asfar S, Safar H, Khouesheed M, Dashti H, Al bader A. Would measurement of C reactive protein reduces the rate of negative exploration for acute appendicitis? JR CollSurgEdinb 2000;45:21-24.
18. Erkasap S, Ates E, Ustuner Z, Sahin A, Yilmaz S ,YAsar B. Diagnostic value of interleukin 6 and C reactive protein in acute appendicitis. Swiss Surg 2000;6(4):169-172.
19. Wu HP, Lin CY, Chang CF, Chang YJ, Hunag CY. Predictive Value of C reactive protein at different cut off levels in acute appendicitis. Am J Emerg Med 2005;23(4):449-453.
20. Paajanen H, mansikka A, Laato M, Kettunen J, Kostiainen S: Are Serum Inflammatory markers age dependent in acute appendicitis? Journal American Coll Surgery 1997;184: 303-308.
21. Eriksson S, Granstorm L, Carlstrom A. The diagnostic value of repetitive preoperative analysis of C reactive protein and total leucocyte count in patients with suspected acute appendicitis. Scand J gastroenterol 1994;29:1145-1149.
22. Andersson RE, Hugander A, Ravn H, Offenbartl K, Ghazi SH, Nystrom PO et al. Repeated clinical and laboratory examinations in patients with an equivocal diagnosis of appendicitis. World J Surg 2000;24:479-485.