Original Article

Diagnostic Utility of White Cell Count, Serum Bilirubin and C Reactive Protein in Acute and Perforated Appendix

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ABSTRACT

Objective: To determine the diagnostic utility of white blood cell count (WBC), serum bilirubin and C-reactive protein (CRP) by to determine perforation in acute appendicitis.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Surgical Department of PIMS Hospital Islamabad from January 2015 to December 2017.

Materials and Methods: This study was conducted on patients undergoing emergency appendectomies. Blood samples were taken from all patients in the first hour of admission for WBC count, serum bilirubin and CRP level and referred to the Hospital laboratory. The appendix specimens submitted in sterile container containing formalin as preservative to histopathology department to assess the inflammatory or perforated appendix as a gold standard. All the data was recorded in the proforma and analyzed by SPSS version 16.

Results: Total 190 patients underwent appendectomies during two year period, their mean age was 26.59±8.78 years and males were in majority.23(12.1%) patients were diagnosed with perforated appendix by histological examination. Mean of serum bilirubin, WBC and CRPl evels were significantly higher among perforated appendix as compare to inflammatory appendix (P-value 0.001). Logistic regression analysis with forward selection shows that serum bilirubin, WBC and CRP was significant factors of the perforated appendix according to histopathology findings ($p<0.05$).

Conclusion: It was concluded that WBC, Bilirubin, and CRP are the best diagnostic markers for perforated appendix. Suspected appendicitis patients with significant raised CRP, WBC and bilirubin suggests that the patients are unsuitable for conservative treatment.

Key Words: Diagnostic utility, WBC, Serum bilirubin, C-reactive protein, appendicitis

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INTRODUCTION

Acute appendicitis is a commonest abdominal emergency and appendectomy is a very common emergency operation performed worldwide[1]. Acute appendicitis is disease of teenager and is rare in infants and elderly peoples. Lifetime threat for acquiring appendicitis testified to be about 7 to 10 %[1,2]. The prevalence of acute appendicitis is the same among females and males before puberty. Among young adults and teenagers, the male to female ratio elevates to 3:2 at the age of 25; later, the higher prevalence among males declines [1,3]. The diagnosis of perforated appendicitis is based upon imaging modalities, laboratory tests, clinical course and history. Acute appendicitis can present with advanced complications, including lump formation, perforation, and abscess creation.[3,4] The benchmark in the diagnosis of perforated Appendix is histopathology assessment of the specimen following surgical procedure[5].This fact has recuperated the need for further effective application of inflammatory indicators to the institution of diagnosis and its complications. Recently, several fresh inflammatory markers have been practiced for confirming the diagnosis of appendix perforation and its complications[2,4,6,7]. The widely practiced laboratory markers to reinforce the diagnosis are yetthe leukocytes counts, serum bilirubin level and C-reactive protein etc.[6,8,9] Initial margin of peripheral leukocytes due to catecholamine and cytokine release represents leukocytosis in majority of cases with acute appendicitis. Even though leukocytosis is not indicative for any specific disease, its existence is a frequent

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outcome in appendicitis. Leukocytosis along with neutrophil supremacy has been highly prognostic of perforated appendicitis within several studies[4,7]. The specificity and sensitivity values of neutrophil dominance in this study are compatible with the earlier studies. Several scoring methods quote leukocytes count as inflammatory parameter for the assessment of acute appendicitis.[8,9,11] In acute appendicitis, serum bilirubin is not a common significant marker. Though, hyperbilirubinemiais found to be a high specificity marker for studies of perforated appendix[5,7,12]. In appendicitis, compromised appendix wall integrity causes movement of endotoxins and bacteria from appendix lumen into portal system. Inflammatory cytokines can possibly then move to liver, provoking intrahepatic cholestasis. Studies have also exhibited that E. coli endotoxin triggers cholestasis depending upon dose,[10,13] which would clarify our outcomes of raised bilirubin levels with increasing severity if appendicitis. Bilirubin can possibly be raised in further sources of gram-negative associated sepsis, which can possibly be of abdominal origin (E. coliin diverticulitis) or from further sources for example pyelonephritis, endocarditis, pneumonia and soft-tissue abscesses[1,14,20] In acute appendicitis occlusion of appendicular lumen results in the mucosal disruption and damage of blood flow. Afterwards, bacteria proliferate and leukocytes infiltration develops in this malfunctioningsite. Migration of WBCs to targeted tissues leads to the liberation of cytokines such as CRP[10,15,16].C-reactive protein, an acute phase protein produced in liver cells, was uncovered in 1930 by Tillette and Francis. Synthesis of CRP elevates during 4-6 hours following acute tissue impairment or commencement of inflammation and becomes two-fold every eight hours then peaks at around 36–50 hours. Because its half-life is just 4-7 hours, its concentration declines rapidly. Thus, among subjects whose symptoms manifest in the course of<12 hours, it has a rather lower sensitivity.[4,15,17] The morbidity and mortality rates elevate if the surgical intervention delays in perforated appendix. It has been reported that diagnostic aids can noticeably diminish the quantity of appendectomies among subjects without appendicitis, the quantity of perforations as well as the length of time consumed in the Hospital stay[5,21]. No fixed technique is presently available to differentiate uncomplicated from complicated appendicitis preoperatively, although many studies on forecasting perforated appendicitis were published [1,6,18,19]. As acute appendicitis is a surgical emergency and around 16 to 17 % cases are complicated by perforation that is correlated with high risk of complications and morbidity. So these biomarkers assign risk and assist the clinicians in diagnosing the appendicitis specially severity prediction i.e. perforation.[4,20-22]

MATERIALS AND METHODS

This prospective study was conducted in department of general surgery at Pakistan institute of medical sciences Islamabad from January 2015 to December 2017. Well-versed consent was taken. All the patients underwent appendectomies after taking informed consent were included. Complete medical history and clinical examination were carried out. Patients who underwent conservative management based on the surgeon's decision, histopathology report shows normal appendix, having hematological disorder and hepatobiliary disorder were excluded. Blood samples were taken from all patients in the first hour of admission for WBC count, serum bilirubin and CRP level Hospital laboratory. Quantitative CRP concentration measured by immuneturbidometry by an experienced laboratory technologist. After surgeries, appendix specimens submitted in sterile container containing formalin as preservative to histopathology department. Data was collected through structured Performa. Data was analyzed using SPSS-16.

RESULTS

The study consisted of 190 patients. The mean age of the patients was 26.590 ±8.787years.There were 96 (50.52%) males and 94(49.47%)females. Out of 190, 167(87.89%) had acute inflammation of appendix and 23 (12.10%) patients were found to have perforated appendix. Overall mean of white blood cell count was $15.92\pm22\times10^9$/L. Serum bilirubin mean was 0.551±0.30mg/dl and the overallmean of c reactive protein was 10.07±19.52 mg/l (Table 1).

There was no significant difference in histopathological findings according to gender (P-value 0.866). Mena of WBC was significantly higher $18.85\pm1.96\times10^9$/L among perforated cases in contrast to patients had inflammatory appendix $15.60\pm1.99\times10^9$/L, p-value 0.001. Serum bilirubin level was high 1.11±0.59 mg/dl in perforated appendix cases as compare to patients having inflammatory appendix 0.51±0.45 mg/dl, these findings were statistically significant, p-value 0.001. C-reactive protein was also, markedly high among perforated patients as; 51.83±32.40 mg/l as compare to patients had inflammatory appendix as 4.32±4.47 mg/l, p-value 0.0001, (Table 2).

To identify the intention and power of our covariates we applied logit regression model with forward selection method. In the final model, which was set on step 3 was in (Table 3). In the final logit model age was not included, as age was dropped at first stage with β= 0.036 (p value= 0.850). With the above logit model, we can predict inflamed and perforated appendix correctly with high accuracy up to 98.4%. The Nagelkerke R square of our logit model was 0.858,

which tells us that the final logit model explained approximately 85% variation of histopathology results.

Table No.1: Descriptive analysis of Quantitative variables n=190

Variables		**Frequencies**	**%tage**
Gender	Male	96	50.5
	Female	94	49.5
Histo-pathology	Inflamed	167	87.9
	Perforated	23	12.1
CRP categories	Less or equal to 20	170	89.5
	More than 20	20	10.5
	Mean ± Standard deviation		
Age	26.59±8.78 years		
White cell count	15.92±2.200 $\times 10^9$/L		
Serum bilirubin	0.551±0.308 mg/dl		
C-reactive protein	10.07±19.53mg/l		

Table No.2: Comparison of gender, CRP, WBC and serum Bilirubin according to histopathology n=190

Variables		**Histopathology findings**		**P value**
		Inflamed	Perforated	
Gender	Male	84	12	0.866
	Female	83	11	
		Mean ± Standard deviation		
White cell count		15.60±1.99$\times 10^9$/L	18.85±1.96$\times 10^9$/L	0.001
Serum bilirubin		0.51±0.45 mg/dl	1.11±0.59 mg/dl	0.001
C-reactive protein		4.32±4.47 mg/l	51.83±32.40 mg/l	0.001

Table No.3: Final logit model with their p values n=190

covariates	**Estimates**	**P value**
Constant	-20.287	0.000
Serum bilirubin	3.243	0.039
WBC (in thousands)	0.806	0.004
CRP	0.135	0.000

DISCUSSION

Acute Appendicitis is a commonest cause of sprouting surgical intervention in teen agers or adolescents[5]. Diagnosis is usually based upon physical evaluation, medical historyand investigations like high WBC count, elevated serum bilirubin, CRP level, ultra-sonography (USG) signs and CT scan abdomen are used in confirmation diagnosis of the disease and its complications[1,5]. Diagnosis establishment is problematic especially in teen-age (females) group and pregnant patients[4,6]. In this study male to female ratio among patients who presented with acute appendicitis in this study was 1:1. This was comparable to the study ofBuckiusetal[10].

In this series mean age of patients was26.59±8.78 years, this is similar a study conducted by J.A Shelton et al.where mean age was 32 years [19].In another study conducted by Mohamed Amine Msolli etal. found similar result, which waspatients mean age 28 ± 3 years with limits formeightto 85 years. Young aged patients under 30-yearand males were in majority[4]. One local study conducted by Tanveer Ahmad et al. mentioned incidence of perforated appendix is higher in males (69.17%) as compared to females (30.82%)[24.] In the present study, perforated/gangrenous appendix was found in 52.2% of males and in 47.8% of females with acute appendicitis. The rate of appendicular perforation fluctuated between 5.5 and 17.0% in different studies while in our study it is 12.1% [6,7.15,17]. Male female ratio presented is almost equal in acutely inflamed appendix and perforated appendix in this study.

In this study WBC count was found between 9000 to 23000 $\times 10^9$/L in patients operated for acute appendicitis while 15.605±1.995$\times 10^9$/L, 16 (Mean ± Standard deviation, median) in inflamed appendix and 18.222± 2.2907$\times 10^9$/L, 19.5 was identified in perforated appendix. SushruthS et al[25] found similar findings, but in his study he compared inflammatory appendix with normal appendix. In a similar study by Sheikh MuzamilShafi et al., they found that WBC raised and sensitivity and specificity of WBC were 97.82% and 55.55%the PPVs for WBC were 91.8%.[12] In another retrospective study carry out by AnshumanSengupta et al. found that for the same cut off value WBC alone had a high NPV of 95% for acute appendicitis. Though, no subjects with both values in typical range had acute appendicitis, providing sensitivity and a NPV of 100% each.[23]

The mean levels of bilirubin were greater for cases with perforated acute appendixthan those with inflamed appendix (0.517 ±0.455mg/dl vs 1.111±0.592d/l, $p<0.001$). Andrew Emmanuel et al. established that hyperbilirubinaemia had a high specificity of 88.0% and PPV of 91.0% for simple acute appendicitis[27]. In his study, hyperbilirubinaemia (>1.0mg/dl) was seen in 69.2% of cases with appendicitis than the cases with complicated appendicitis 78.4% had hyperbilirubinaemia. Abouzeid AE al[26] also found similar findings. The specificity and sensitivity of bilirubin (>1.0mg/dl) as a predictor of complicated appendicitis were 78% and 33.9%, respectively[27].Another study conducted by D'Souza Nshows hyperbilirubinaemia in simple appendicitis vs. perforated appendicitis, had a specificity of 0.82 for perforated appendicitis, odds ratio of 10.8 and a

sensitivity of 0.70. Comparing serum bilirubin to CRP and WBC in perforated appendix, bilirubin had a higher specificity (0.82) as compared to both CRP (0.21) and WBC (0.34), however a lower sensitivity (0.70 vs0.95 and 0.80 respectively)[21].

In this study acute appendicitis the C-reactive protein was 4.32±4.47 mg/l, and in perforated appendix it was higher 51.830±32.40 mg/l. The utility of CRP in diagnosing of appendicitis had evaluated in many studies. Negative CRP levels would most likely be associated with normal appendix [17]. In contrary, Amalesh T et al. exhibited that the sensitivity, specificity, PPV, and NPV for CRP in appendicitis was 91%, 42%, 88%, and 48%, respectively, and that it may not be a useful tool to surgeons [22]. When CRP taken alone, the PPV was 94.7%, specificity was 72%, and sensitivity was 85.1% in a study done by Shefki Xharra et al [11].

CONCLUSION

It was concluded that markedly elevated WBC, Bilirubin, and CRP are the non-invasive and best diagnostic toolsfor perforated appendix. Suspected appendicitis patients with significant raised CRP, WBC and bilirubin suggests that the patientsare unsuitable for conservative treatment.

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Author's Contribution:

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