

**Original Research**

**Role of Serum C-Reactive Protein and White Blood Cells in the Diagnosis of the Patients with Suspected Appendicitis: A Prospective Cohort Study**

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**ABSTRACT:**

Uses of some laboratory investigations in the diagnosis of patients with suspected acute appendicitis have been widely used. However, white blood cell count (WBCC) and C-reactive

114



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protein (CRP) were routine requested in patients with suspected appendicitis. This work of prospective study aimed to assess the useful of WBCC and CRP value in diagnosis of patient with suspected appendicitis. A prospective cohort study were performed. WBCC and CRP were measured prospectively in patients presenting with lower right abdominal pain at the surgery department of Alwahda hospital in Derna city. The results were correlated with each patient's outcome. It shown that uses of WBCC and CRP tests in combination had sensitivity ( 65% ) ; specificity (75%) ; PV (+) 92.8% and PV (-) 30%. Also CRP had the highest degree of diagnostic accuracy than WBCC {sensitivity, 81.2%; specificity, 68.7%; PV (+), 92.8%; PV (-), 42.3% & sensitivity, 72.5%; specificity, 50%; PV (+), 87.8%; PV (-), 26.6% }, respectively. Despite of that the result may have an important clinical and economic implication. The diagnosis of appendicitis should be mainly depended on clinical examination finding and include others helpful investigations such as Ultrasound and CT scan.

**KEYWORDS:** White Blood Cell Count, C-Reactive Protein, Appendicitis.

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## INTRODUCTION

Acute appendicitis (AA) is one of the most cause of abdominal pain that may need urgent surgical intervention (1). It has been reported that 16% of people of western country may expose to acute appendicitis at some point of their life (2).

The classical symptoms of Acute appendicitis (AA) were fever, vomiting, right iliac fossa pain (3). In acute appendicitis, the appendicular lumen occlusion causes blood flow impairment and mucosal disruption that led to bacteria proliferation and leukocyte infiltration at the defective site that result in releasing of serum inflammatory markers. The

Diagnosis of Acute appendicitis (AA) is some time confused with others diseases and it is mainly depended on the medical history, clinical evaluation of the patients, and the surgeon experience. There are some others investigations that may useful in diagnosis of Acute appendicitis (AA) like ultrasound and computed tomography (CT), (4,5). The early diagnosis of Acute appendicitis (AA) is very

important because delay of the diagnosis may lead to serious complication. Recent researchers have deeply focus on others investigation that may aid surgeon to have an accuracy diagnosis of appendicitis. These investigations include simple blood tests like white blood cell count (WBCC) and C-reactive protein (CRP).

Useful of CRP in diagnosis of Acute appendicitis (AA) had shown sensitivities rates from 40% to 94% and specificities of 38% to 87% (6,7). Other studies had correlated a high value of CRP with some serious complications like perforation and appendix abscess (8,9). These studies were retrospective studies in their design that depend on patients record as a source of data collection.

Data from prospective study design were limited and some of these studies had report high sensitivities and specificities of CRP values (83% to 96%, and 87% to 94%), respectively (10,11). Due to the shortage of data from prospective studies, the aim of our prospective study was to assess the useful of WBCC and CRP value in diagnosis of patient with suspected appendicitis.

*Hussien et al., 2025*

## **MATERIALS AND METHODS**

### ***Study Design***

This is a prospective cohort study. WBCC and CRP were measured prospectively in patients presenting with lower right abdominal pain at the surgery department of Alwahda hospital in Derna city.

All patients presenting to surgical department at Alwahda hospital with lower right abdominal pain from December 2020 to December 2021 were randomly included in this study. All clinical data were collected prospectively and all patients with suspected acute appendicitis have WBCC and CRP measurements as routine. All data including the demographic information, history, physical examination, and laboratory data such as leukocytosis and CRP will gather from the all participants. Patient's data were directly recorded on special forms that are designed for this study.

Informed consent was taken from all participants' patients or parents if patient were child. Diagnosis of AA will be written in the USG Report as favor to have AA or negative to have AA than we will compare the WBCC and CRP results with surgical finding result that will write in postoperative form as "acute appendicitis" or "gangrenous appendix" and/or normal appendices. Sensitivity, specificity and positive and negative predictive values for WBCC and CRP individually and in combination with one another will be carry out. A positive WBCC was taken as being  $\geq 11 \times 10^3/L$  for WBC counts and  $\geq 1.17$  mg/dL for CRP. We consider a negative result for either values or one of them had negative result and a positive result for both values had positive result when two tests are in combined.

### ***Study Location***

This study was undertaken in the surgical department at Alwahda Hospital, Derna city, Libya.

### ***Statistical Analysis***

The statistical analysis was achieved by using the Statistical Package for social Sciences; SPSS version 22.0 (SPSS Inc., Chicago, IL). Collected data were analyzed with applying appropriate statistical tests, at p value of  $<0.05$ .

## **RESULTS**

The mean age of our sample was 14.32 years with SD 8.6 (range of age was 3-50 years). It shows that the age was significance difference between both genders with p-value 0.013 using T-test (mean age for male 11.6 years with SD 5.8 and for female 15.9 with SD 9.6). Out 106 (66 females and 44 males) patients with suspected of acute appendicitis, 96 underwent an operation for suspected appendicitis (appendectomy). 16(16.7%) had a diagnostic on opening surgery with a normal appendix, 59(61.5%) had acute appendicitis, 12(12.5%) had gangrene, and 9(9.4%) had perforated appendicitis, figure (1). All patients who underwent surgery were discharged home and remain observational patients (10 pts.) were referred to other specialties such as gynecology and urology for further evaluations. This study showed a high positive predictive value of 87.8% for a raised WCC (table1) and 92.8% for a raised CRP level (table2) in patients with appendicitis. The positive predictive values keep high to a value of 92.8% when both parameters were raised (table3). It also shows a low negative predictive value for WCC, CRP, and

combined both tests (26.6%, 42.3%, and 30%), respectively for acute appendicitis patients.

**Validity of White Blood Cell Count (WBCC) measurement:** As shown in table (1).

#### *Sensitivity of the Test*

It shows that probabilities of having positive test result ( $\geq 11 \times 10^3/L$ ) among those who confirm to have appendicitis after appendectomy are high (72.5%).

**Specificity of the test:** It shows that probabilities of having negative test result ( $< 11 \times 10^3/L$ ) among those who confirm to do not have appendicitis after appendectomy are in the middle way (50%).

It shows that 30 patient who had normal range result for WBCC underwent surgery for appendectomy. 22 out of 30 patients (73.3%) confirmed to have acute appendicitis, while 8 out 30 patients (26%) confirmed to have normal appendix on histopathology result.

#### *Validity of C-Reactive Protein (CRP) measurement*

As shown in table (2). It shows that CRP test has highest degree of diagnosis accuracy than WBCC (table 2A).

#### *Sensitivity of the Positive Test*

It shows that probabilities of having positive test result of CRP among those who confirm to have appendicitis after appendectomy are very high (81.2%).

#### *Specificity of the Negative Test*

It shows that probabilities of having negative test result of CRP among those

who confirm to do not have appendicitis after appendectomy are high (68.7%). It shows that 26 patients who had normal range result for CRP underwent surgery for appendectomy. 15 out of 26 patients (57.6%) confirmed to have acute appendicitis, while 11 out 26 patients (42.3%) confirmed to have normal appendix on histopathology result.

#### *Measures the Validity of White Blood Cell Count (WBCC) and C-Reactive Protein (CRP) tests in combined together:*

As shown in table (3).

#### *Sensitivity of the Positive Test*

It shows that probabilities of having positive test result for both WCC&CRP values among those who confirm to have appendicitis after appendectomy are high (65%).

#### *Specificity of the Negative Test*

It shows that probabilities of having negative test result for both

WCC&CRP values among who confirm to do not have appendicitis after appendectomy are high too (75%). It shows that 40 patient who had negative result for WCC & CRP were underwent surgery for appendectomy. 28 out of 40 patients (70%) confirmed to have acute appendicitis, while 12 out 40 patients (30%) confirmed to have normal appendix on histopathology result.

#### *Prediction of complication (Gangrene and Perforation)*

As show in tables (4,5,6). They had shown that the 12(15%) patients and 9 (11.25%) patients had surgical

complications such as gangrene and perforation respectively when their WCC and CRP value were raised individually or together.

The mean value of WCC was (16444.44) almost in both surgical complication-finding patients (gangrene & perforation).

The mean age for patients who had gangrene and perforated were {15.7 years with SD13.55, &12.1years with SD13.9} and the most common effected gender was male {7 (58.3%), 5 (55.6%)}, respectively.

**Table (1) Sensitivity, Specificity, Positive Predictive Value (PV+) and Negative Predictive Value (PV-) for White Cell Count {n = 96}.**

C-Reactive protein Test	Appendicitis		Total
	Yes	No	
<b>Positive**</b>	65	5	70
<b>Negative*</b>	15	11	26
<b>Total</b>	80	16	96

\*A negative result for value ( $<11 \times 10 /L$ ); \*\*A positive result for values. ( $\geq 11 \times 10 /L$ ).

For acute appendicitis (%): Sensitivity= (72.5%); Specificity= (50%); PV (+) = (87.8%); PV (-) = (26.6%).

**Table (2) sensitivity, specificity, positive predictive value (PV+) and negative predictive value (PV-) for C-reactive protein (CPR) {n=96}.**

White cell count Test	Appendicitis		Total
	Yes	No	
<b>Positive**</b>	58	8	66
<b>Negative*</b>	22	8	30
<b>Total</b>	80	16	96

This study explained the negative and Positive results for acute appendicitis as the following:

\*A negative result for value; \*\*A positive result for values.

For acute appendicitis (%): Sensitivity= (81.2%); Specificity= (68.7%); PV (+) = (92.8%); PV (-) = (42.3%).

**Table (2A). Comparing Value of WBCC and CRP**

Subject	WBCC	CRP
<b>Sensitivity</b>	72.5%	81.2%
<b>Specificity</b>	50%	68.7%
<b>Positive predictive value (PV+)</b>	87.8%	92.8%
<b>Negative predictive value (PV-)</b>	26.6%	42.3%

**Table (3) sensitivity, specificity, positive predictive value (PV+) and negative predictive value (PV-) for both white cell count and C-reactive protein (CPR) {n=96}.**

C- Reactive protein Test	Surgical complication			Total
	Acute	Gangrene	Perforated	
Positive**	44	12	9	58
Negative*	15	0	0	15
<b>Total</b>	59	12	9	73

**Table (4). Surgical complication for WBCC value**

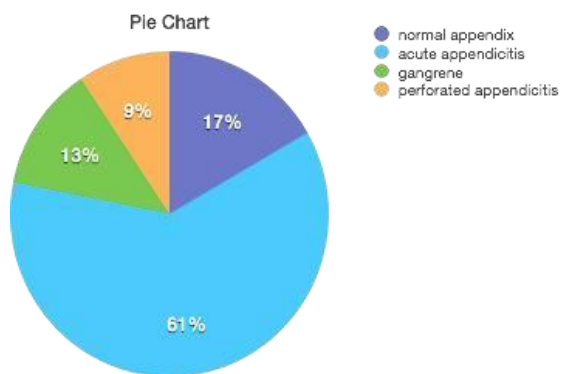
\*A negative result for value, \*\*A positive result for values.

White cell count Test	Surgical complication			Total
	Acute	Gangrene	Perforated	
Positive**	37	12	9	58
Negative*	22	0	0	22
<b>Total</b>	59	12	9	80

**Table (5). Surgical complication for CRP value**

\*A negative result for either values or one of them had negative result, \*\*A positive result for both values had positive result. For acute appendicitis (%): Sensitivity= (65%); Specificity= (75%); PV (+) = (92.8%); PV (-) = (30%).

White cell count & CRP Tests	Appendicitis		Total
	Yes	No	
Positive**	52	4	56
Negative*	28	12	40
<b>Total</b>	80	16	96



**Figure (1) : Surgical finding on open appendectomy.**

\*A negative result for value, \*\*A positive result for values.

**Table (6). Surgical complication for WCC & CRP values**

White cell count & CRP Tests	Surgical complication			Total
	Acute	Gangrene	Perforated	
Positive**	31	12	9	52
Negative*	28	0	0	28
<b>Total</b>	59	12	9	80

\*A negative result for either values or one of them had negative result.

\*\*A positive result for both values.

## **DISCUSSION**

Raised serum inflammatory markers (WBCC & CRP) can be used in diagnosis of patients with suspected acute appendicitis. Our study result has an agreement with other studies that support of presence of serum inflammatory markers more likely to predict a specific diagnosis such as acute appendicitis, even when one of WBCC and CRP levels is raised (12,13,14). Furthermore, this study also shows that the raised levels of WBCC and CRP could predict the development of a complication such as gangrene or perforation. Our finding shows high sensitivity rate among patients who already confirmed to have an appendicitis when one or both WBCC and CRP levels are raised and this is finding is in contrast with other studies that do not support the presence of inflammatory markers is a good confirmative diagnosis (15,16). The most important finding of this study that, to our knowledge, has not previously been demonstrated is the nearly 93% positive predictive value for acute appendicitis if both WBCC and CRP are raised, it means that any patient who had appendicitis are more likely to have raised values result for both WBCC & CPR values. However, irrespective of this possibility, 28 patients with normal WBCC and CRP needed an appendectomy, and therefore, depending on other clinical criteria, these patients require admission to hospital. Also, our finding shows high specificity rate among patients who already confirmed do not have appendicitis when both WBCC and CRP levels are on the normal range (75%). However, the negative predictive value was very low 30% for both tests were in the normal range and this may have a negative effect to have a trust only on those tests in the diagnosis of appendicitis. Furthermore, it shows that

CRP test has highest degree of diagnosis accuracy than WBCC and this finding has an agreement with other studies (17,18). It is obvious that the careful clinical examination of patients with acute abdominal pain, and particularly suspected appendicitis has more challenges and depend on the surgeon experience and skills. However, supporting investigations likes CT scan and ultrasound may need to help in confirming the diagnosis of some patients, while other cases may need just short time of observation to exclude the appendicitis. Depend on our result, if the clinical findings are obviously clear for patient complained of lower abdominal pain to have possible acute appendicitis, than it should outweigh over other investigations. On the other hand, if the clinical finding is unlikely for the patients to have acute appendicitis and no others symptoms and signs need to be have more evaluated, the presence of a CRP and WBCC values within normal range can reassurance the surgeon and allow the patient to be discharged home. If either or both markers were raised, it would be the right idea to admit the patient for further investigations and observation.

## **CONCLUSION**

Despite of that, the white blood cell count and C-reactive protein measurements are useful in the assessment of acute appendicitis, The diagnosis of appendicitis should be mainly made on clinical examination finding and include others helpful investigations such as Ultrasound and CT scan to support the clinical diagnosis.

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## المخلص

استُخدمت بعض التحاليل المخبرية على نطاق واسع في تشخيص المرضى المشتبه بإصابتهم بالتهاب الزائدة الدودية الحاد. ومع ذلك، يُطلب عادةً إجراء تعداد خلايا الدم البيضاء (WBCC) وبروتين سي التفاعلي (CRP) للمرضى المشتبه بإصابتهم بالتهاب الزائدة الدودية. هدفت هذه الدراسة الاستباقية إلى تقييم فائدة قيم WBCC و CRP في تشخيص المرضى المشتبه بإصابتهم بالتهاب الزائدة الدودية. أُجريت دراسة استباقية على مجموعة من المرضى، حيث تم قياس WBCC و CRP بشكل استباقي لدى المرضى الذين يعانون من ألم أسفل البطن الأيمن في قسم الجراحة بمستشفى الوحدة بمدينة درنة. رُبطت النتائج بحالة كل مريض. أظهرت النتائج أن استخدام اختبارات WBCC و CRP معاً يتمتع بحساسية 65%، وخصوصية 75%، وقيمة تنبؤية إيجابية 92.8%، وقيمة تنبؤية سلبية 30%. كما أظهر CRP أعلى دقة تشخيصية من WBCC (حساسية 81.2%، خصوصية 68.7%، قيمة تنبؤية إيجابية 92.8%). القيمة التنبؤية السلبية (PV) = 42.3%، والحساسية = 72.5%، والنوعية = 50%؛ القيمة التنبؤية الإيجابية (PV) = 87.8%؛ القيمة التنبؤية السلبية (PV) = 26.6%، على التوالي. على الرغم من ذلك، قد يكون لهذه النتيجة آثار سريرية واقتصادية هامة. ينبغي أن يعتمد تشخيص التهاب الزائدة الدودية بشكل أساسي على نتائج الفحص السريري، وأن يشمل فحوصات أخرى مفيدة مثل التصوير بالموجات فوق الصوتية والتصوير المقطعي المحوسب.

**الكلمات المفتاحية:** تعداد خلايا الدم البيضاء، البروتين المتفاعل C، التهاب الزائدة الدودية.

