



## Evaluation of Diagnostic Accuracy of C - reactive protein and Leucocyte Count in Operated Cases of Suspected Acute Appendicitis

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### ABSTRACT

#### BACKGROUND & OBJECTIVES

Acute appendicitis is the most common cause of acute surgical abdomen and appendectomy is the most commonly done emergency surgery. The rate of negative appendectomy remains 15-30%. This study evaluates the diagnostic accuracy of C-reactive protein and WBC count in operated cases of suspected acute appendicitis.

**METHOD :** Between July 2018 and July 2020, 75 patients operated for acute appendicitis were studied. Preoperatively blood for CRP, WBC count & DC was collected and post operatively histopathological reports were collected. WBC count and CRP were correlated with HPE reports.

**RESULTS:** In patients with histopathologically proven appendicitis, CRP levels and WBC level were significantly raised ( $P = 0.04923 > 0.025$  and  $P = 0.11439 > 0.025$  respectively). Serum CRP level was normal in all 12 cases of histopathologically normal appendix. The sensitivity and specificity of CRP were 73% and 100% respectively.

**CONCLUSION :** CRP is helpful in diagnosis of acute appendicitis. Normal preoperative serum CRP measurement in patients with suspected acute appendicitis is most likely associated with a normal appendix. By avoiding surgery in such cases we can decrease the rate of negative appendectomy.

**KEY WORDS :** CRP, Acute appendicitis, WBC count, Histopathological report.

### I. INTRODUCTION

Acute appendicitis is the most common cause of acute surgical abdomen<sup>1</sup> and appendectomy is the most commonly done emergency surgery.

Acute appendicitis, when presenting in a teenager and with a classical history, presents the surgeon with little by way of a diagnostic challenge. However, this disease is notorious in its ability to simulate other conditions and in the

frequency with which it too can be imitated by other pathologies<sup>2</sup>.

It is often and reasonably said that, to remove a normal appendix when some other condition, which does not require surgery is present is not blameworthy. In general this is true, because to do so guards against the other error of failing, on account of confusing the diagnosis with something else and then having to remove the appendix at a later stage in the face of greater risk of complications, morbidity and even death<sup>2</sup>.

Nevertheless, unnecessary appendectomy is not altogether without problems. There will be a small incidence of wound sepsis and the subsequent adhesive intestinal obstruction and incisional hernia. More important is the situation where the operation fails to relieve the patients symptoms and so has wasted everyone's time and, in addition caused him (or more her) inconvenience and suffering without therapeutic gain<sup>2</sup>. The emergency surgeon must also remember that "one can't step twice into the same river" and that the patient with acute right iliac fossa pain, and a scar into the bargain, is not the same patient psychologically or physically as before. Finally, there is the economic argument that an unnecessary appendectomy is a waste of scarce resources.

It used to be taught that the unnecessary appendectomy rate should be around 20% in order to reduce the chance of missing a possible inflamed appendix. Since the mid 1980's this has no longer held true and with the incorporation of adjuvant techniques to improve diagnosis and decision making, the error rate has been significantly reduced<sup>3</sup>.

Even with all the investigations, the negative appendectomy rate is 15-30% (more in females and in extremes of age)<sup>4</sup>.

Accuracy rates in diagnosis of appendicitis are variable. The role of blood tests, radiological investigations, laparoscopy and computer analysis has been studied.



Additional tests that would improve the diagnostic accuracy and reduce the number of unnecessary operations are needed. This is particularly important in these days where health planning is driven by cost containment.

C - reactive protein was recognized in 1930 and is an ubiquitous acute phase reactant produced as a non-specific response to an acute inflammatory stimuli. Many reports have investigated the value of raised serum CRP measurement in improving the diagnosis of acute appendicitis, with controversial reports<sup>5</sup>.

The total leukocyte count (WBC) is widely used to aid the diagnosis of acute appendicitis, although this is controversial. Of patients with acute appendicitis 79.90% have a raised WBC count ( $> 10,000/\text{mm}^3$ ), Neutrophilia of  $> 75\%$  is observed in 78% of patients<sup>6</sup>.

A raised WBC count is a sensitive test for acute appendicitis, but is not diagnostic because of its relatively low specificity and does not contribute to management in patients with unequivocal clinical findings.

Some observers have noted that sequential total white cell counts may be useful as the total count remains high in acute appendicitis, but falls in those without appendicitis<sup>6, 17</sup>.

It is not unusual to find an inflamed appendix or perforated appendix with normal leukocyte count<sup>1, 6</sup>.

In this study we correlated the serum levels of CRP, WBC count and raised neutrophil count with histopathology of the removed appendix.

We would like to know whether a normal CRP, WBC count and raised neutrophil count would exclude the presence of acute appendicitis.

## II. AIMS AND OBJECTIVES

To analyze the diagnostic accuracy of C-reactive protein and leukocyte count in patients operated on for suspected acute appendicitis.

## III. REVIEW OF PRESENT STUDY

Marchand et al<sup>7</sup>, studied 106 patients admitted to the emergency room with a tentative diagnosis of acute appendicitis and who subsequently underwent appendectomy. They concluded that the cytochemically determined neutrophil count, when greater than the upper limit of the reference interval of either 75% or  $7.88 \times 10^9/\text{L}$ , and the total white blood count greater than

the upper limit of reference interval of  $10.5 \times 10^9/\text{L}$  were single best tests for diagnosis of acute appendicitis with the highest sensitivities of all tests examined (81-84%). The manual differential count and C- reactive protein showed significantly lower sensitivities.

They also suggested that the combination of these tests has 100% sensitivity and 50% specificity in diagnosis of acute appendicitis.

Mikaelsson and Arnbjornsson<sup>8</sup> studied the clinical usefulness of preoperative determination of C - reactive protein (CRP) in patients with suspected acute appendicitis in 156 patients undergoing appendectomy. CRP values were found to increase with an advancing stage of the appendicitis found at operation and the length of the preoperative phase of illness.

Peltola et al<sup>9</sup> studied 162 children with suspected acute appendicitis and concluded that the predictive value of combined positive CRP and WBC tests was not less than 93%.

Norback and Harju<sup>10</sup> studied the role of the common parameters of inflammation in the diagnosis of acute appendicitis measuring axillary temperature, blood leukocyte and lymphocyte fraction, serum C-reactive protein (CRP) and ESR in 354 patients with clinical diagnosis of acute appendicitis. 37 patients had normal leukocyte and lymphocyte fraction, CRP and their HPE was negative for appendicitis. He concluded that if laparotomy was avoided in these 37 patients, half of the unnecessary operations could have been avoided, there by reducing the negative appendectomy rate.

Thimsen et al<sup>11</sup> studied 70 suspected cases of acute appendicitis and concluded that a normal CRP value in a patient presenting with symptoms for more than 12 hours, does not have acute appendicitis and can be followed in an outpatient setting.

## DIFFERENTIAL DIAGNOSIS

Although acute appendicitis is the most common abdominal emergency, the diagnosis at times can be extremely difficult. There are a number of common conditions that it is wise to consider carefully and, if possible exclude. The differential diagnosis differs in patients of different ages. In women, additional differential diagnosis is involvement of the genital tract.



CHILDREN	ADULTS	ADULT FEMALE	ELDERLY
Gastro enteritis Mesenteric adenitis Meckel's diverticulitis Intussusception Henoch Schonlein purpura	Regional enteritis Ureteric colic Perforated peptic ulcer Torsion testis Pancreatitis Rectus sheath haematoma	Mittelschmerz Pelvic inflammatory disease Pyelonephritis Ectopic pregnancy Torsion/rupture of ovarian cyst Endometriosis	Diverticulitis Intestinal obstruction Colonic carcinoma Torsion appendix epiploicae Mesenteric infarction Leaking aortic aneurysm

**IV. MATERIAL AND METHODS**

This study was performed on 75 patients admitted to B.L.D.E.A's Shri.B.M.Patil Medical College Hospital and Research Centre, Bijapur, over a period of 2 years from July – 2003 to July – 2005 . These patients were diagnosed to have acute appendicitis and were operated on the same day.

**INCLUSION CRITERIA**

All patients admitted with acute abdominal pain and clinically diagnosed as acute appendicitis and posted for surgery.

**EXCLUSION CRITERIA**

Acute appendicitis patients with associated diseases like,

1. Rheumatoid arthritis
2. SLE
3. Glomerular nephritis
4. Gout
5. Inflammatory bowel disease.
6. Malignant neoplasm
7. Myocardial infarction
8. Any other conditions where CRP was raised.

Pre-operative investigations were done which included WBC count and CRP levels. WBC count of more than 10,000 cells/mm<sup>3</sup> was

considered positive and neutrophil count of more than 75% was considered positive.

2ml of plain blood was collected and serum was used for the study. No special preparation of the patient was required prior to sample collection by approved techniques. When there was delay, the sample was stored at 2-8° C. Maximum period of storage was 72 hours.

The materials provided with CRP kit were reagent pack and an accessories pack. The reagent pack comprised of Rhelax CRP latex reagent, positive control and negative control. The accessories pack comprised of glass slides with six reaction circles, sample dispensing pipettes, mixing sticks and rubber teat.

helax CRP slide test for detection of CRP is based on the principle of agglutination. The test specimen (serum) was mixed with rhelax CRP latex reagent and allowed to react for 2 minutes after mixing. Appearance of macroscopic agglutination was taken as positive. The absence of visible agglutination and the presence of opaque fluid constituted a negative reaction. When CRP levels were more than 6 mg/dl agglutination occurs and it was taken as positive result.

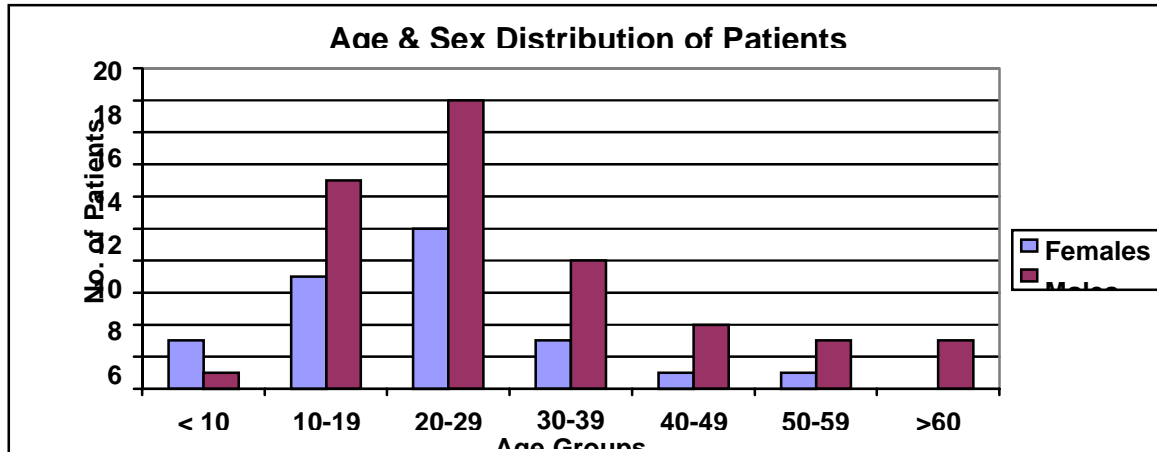
Post operative histopathology specimen was reported by senior pathologist of the department.



## V. OBSERVATIONS AND RESULTS

TABLE 1  
Age and Sex distribution

Age in Years	Females	Males	Total
< 10	3	1	4
10 – 19	7	13	20
20 – 29	10	18	28
30 – 39	3	8	11
40 – 49	1	4	5
50 – 59	1	3	4
> 60	0	3	3
Total	25	50	75

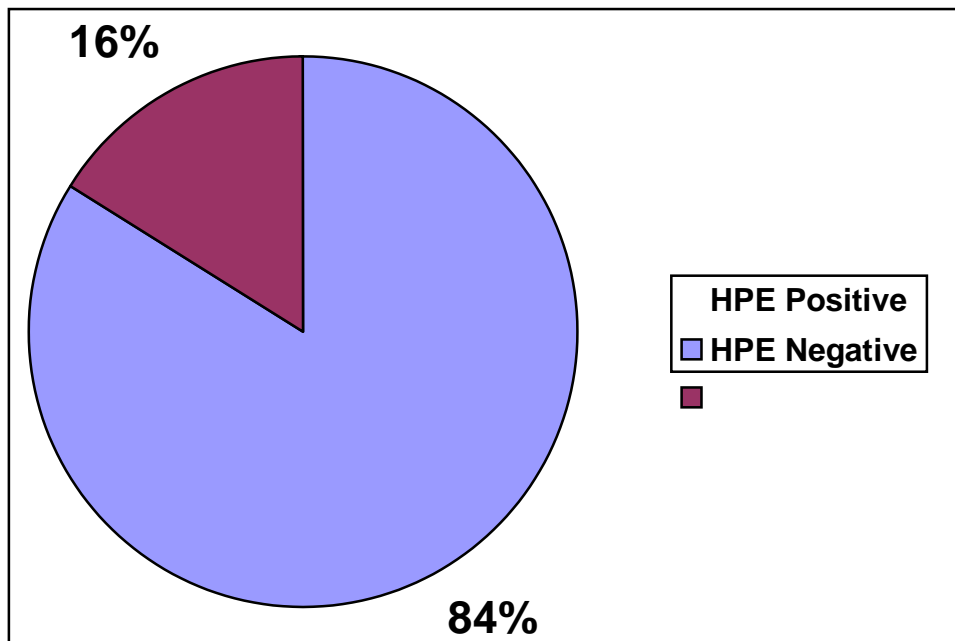


A total number of 75 cases of acute appendicitis, out of them, 25 were female and 50 were male. Patient's age group ranged from 6 years to 65 years. Maximum group of patients belonged to 20 – 29 years.



TABLE 2  
Distribution of histopathologically positive and negative cases.

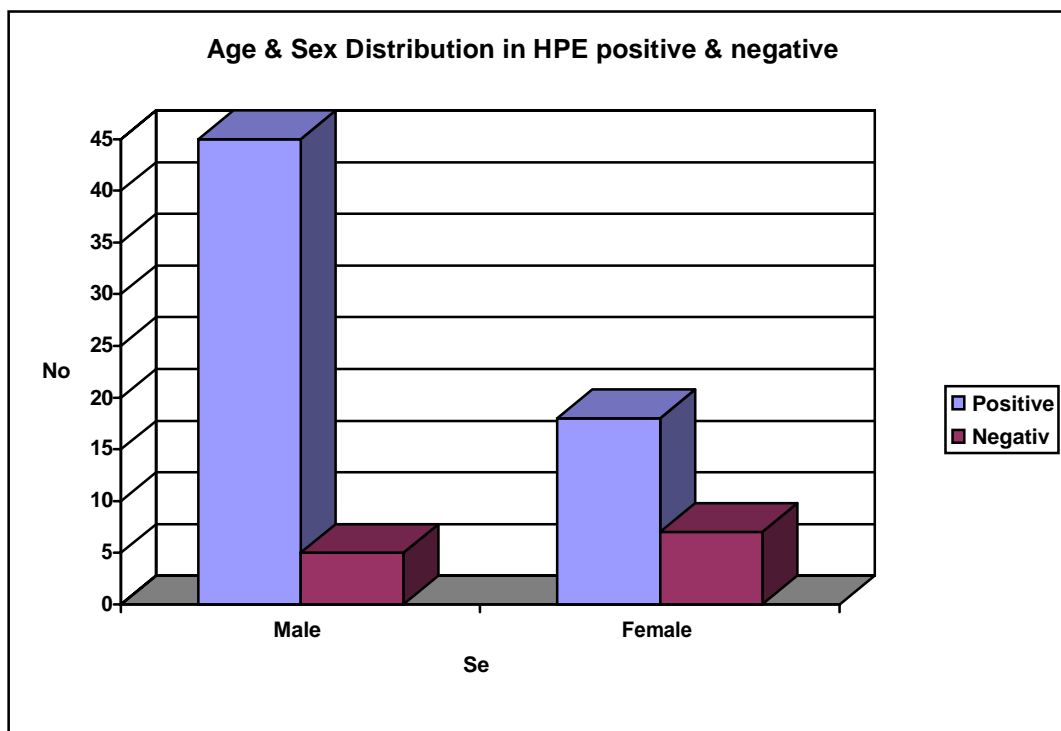
Total No of cases	75	Percentage
HPE Positive	63	84%
HPE Negative	12	16%



Out of 75 cases studied, 84% of the cases were histopathologically positive and 16% of cases were histopathologically negative, so the negative appendicectomy rate in our study is 16%.

TABLE 3  
Age and sex distribution in correlation to histopathologically positive and negative cases.

Type (HPE)	No	Female	Males
Positive	63	18(28.5%)	45(71.4%)
Negative	12	7(58.33%)	5(41.66%)
Total	75	25	50

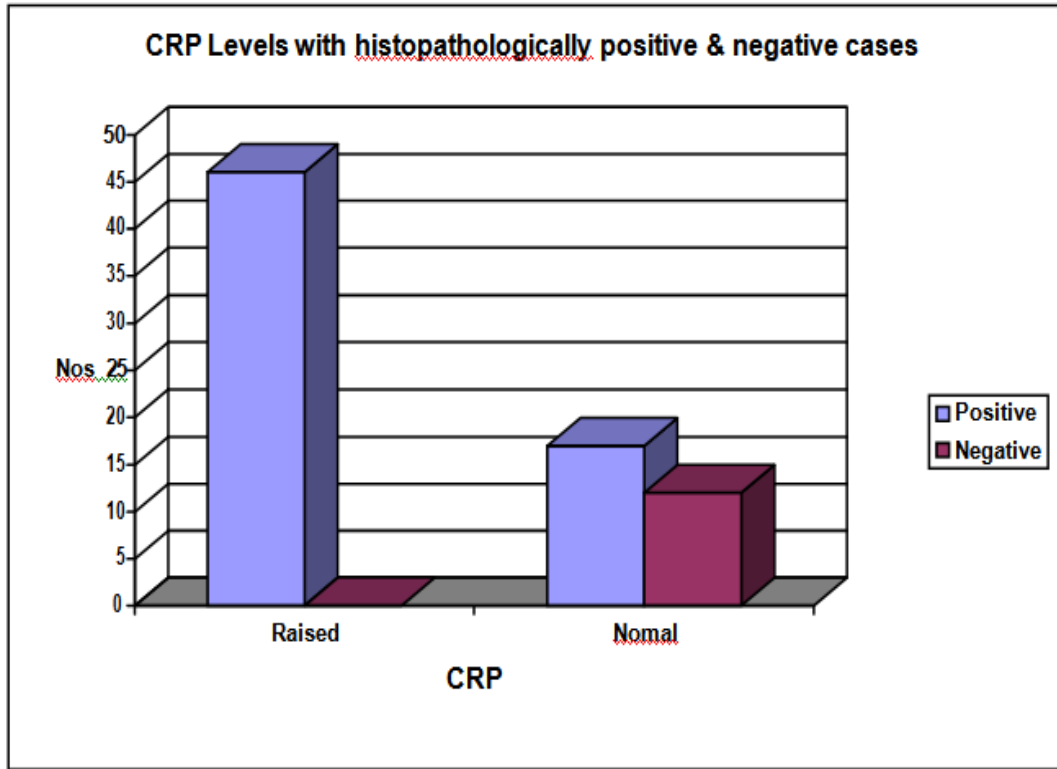


28.5% of HPE positive patients were females and 71% were males. Among HPE negative, patients 58% were females and 42% were males.

**TABLE 4**

Correlation of CRP levels with histopathologically positive and negative cases.

HPE	CRP		TOTAL
	RAISED	NORMAL	
Positive	46(73%) TP	17 (27%) FN	63
Negative	0 FP	12 (100%) TN	12
Total	46	29	75



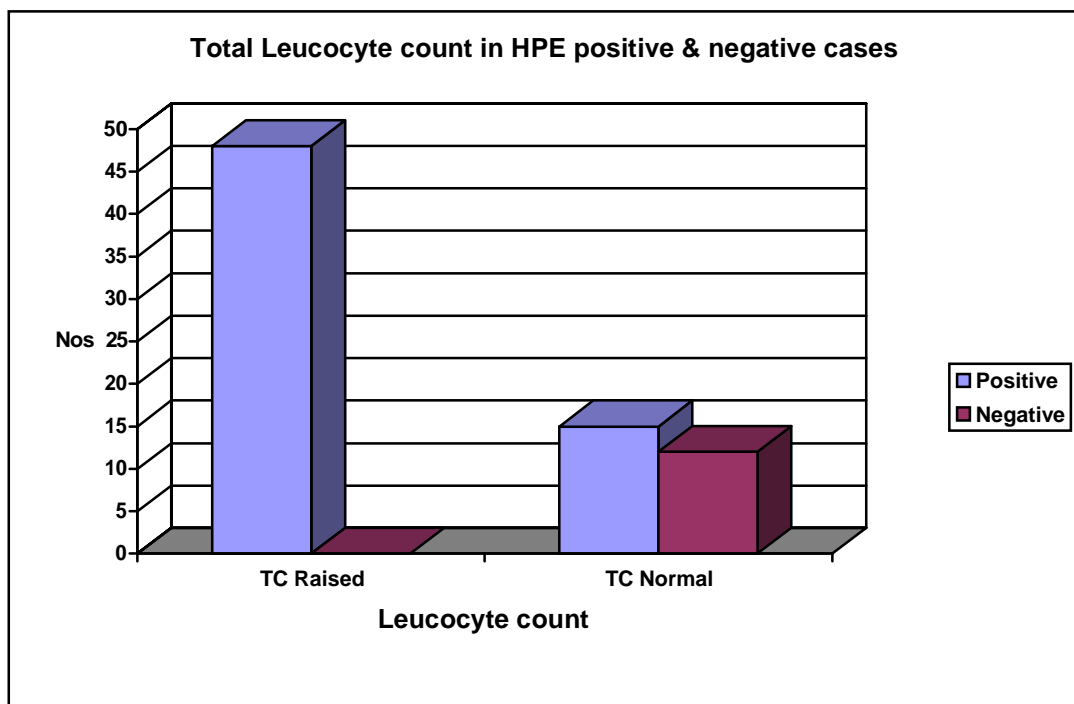
Sensitivity-73.01% Specificity-100%  
 Predictive value of positive test-100% Predictive  
 value of negative test-41.37% Accuracy-77.33%  
 The result of  $p = 0.04923 > 0.025$  (Z test for  
 difference of proportions).

HPE positive patients 46(73%) had raised CRP and  
 17(27%) had normal CRP. Among 12 cases which  
 were HPE negative none of them had raised CRP  
 and all 12(100%) had normal CRP. Sensitivity,  
 specificity, predictive value of positive test &  
 negative test and accuracy of raised CRP levels are  
 as shown earlier.

CRP level was raised in 46(61%) cases  
 and was normal in 29(39%) cases. Among the 63

**TABLE 5**  
 Correlation of total leucocyte count with histopathologically positive and negative cases.

Type (HPE)	WBC		Total
	TC-Raised	TC-Normal	
Positive	48 (76%)	15 (24%)	63
Negative	0	12 (100%)	12
Total	48	27	75



Sensitivity -76.19%  
 Specificity – 100%

Predictive value positive test -100% Predictive value of negative test – 44.44% Accuracy – 80%

The result of  $p = 0.11439 > 0.025$  (Z test for difference of proportions).

In the study population of 75 patients, 63 were

histopathologically proved appendicitis. Among them 46(76%) had raised total leucocyte count and 15(24%) had normal count. Out of 12 histopathologically negative cases all the 12(100%) cases had normal total WBC count.

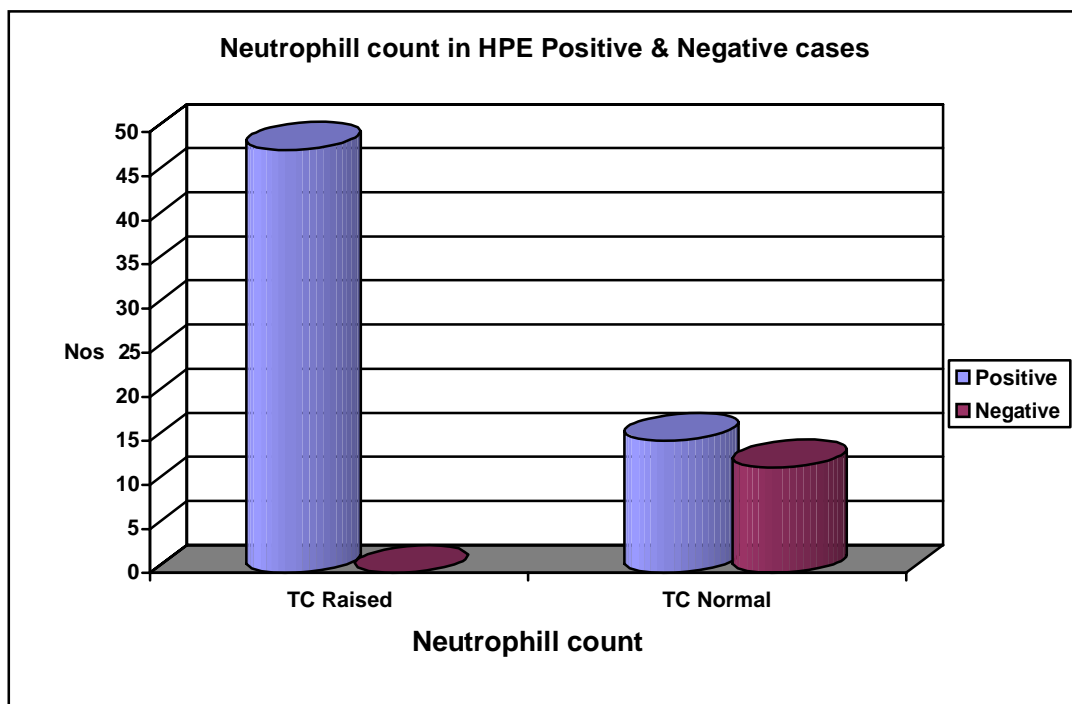
Sensitivity, Specificity, Predictive value of positive test, Predictive value of negative test and accuracy are as shown earlier.

**TABLE 6**

Correlation of Neutrophil count with histopathologically positive and negative cases.

HPE	DC		Total
	(N)Raised	(N)Normal	
Positive	48(76%) TP	15 (24%) FN	63
Negative	0 FP	12 (100%) TN	12
Total	48 (64%)	27 (36%)	75





Sensitivity -76.19%  
 Specificity – 100%

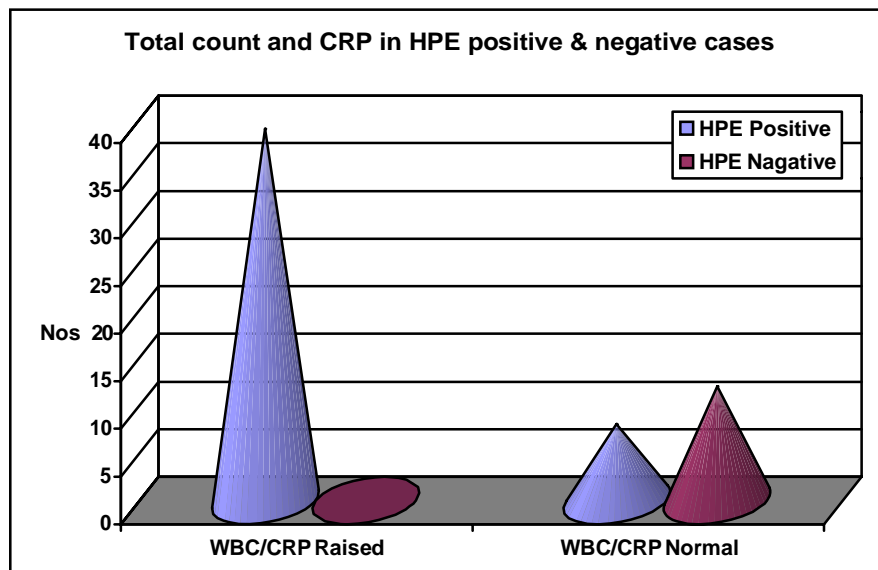
Predictive value of positive test -100% Predictive value of negative test – 44.44% Accuracy – 80%  
 The result of  $p = 0.11439 > 0.025$  (Z test for difference of proportions).

Neutrophilia was seen in 64% of the study population. Neutrophil count was raised in 76% of HPE positive patients and none of the HPE negative cases. Neutrophil count was normal in 24% and 100% cases of HPE positive and negative cases respectively.

**TABLE 7**

Correlation of total leucocyte count and CRP levels in combination with histopathologically positive and negative cases.

WBC/CRP	HPE Positive	HPE Negative	Total
Increased WBC > 10,000 cells/mm <sup>3</sup> CRP > 6mg/dl	39	8	47
Normal WBC < 10,000 cells/mm <sup>3</sup> CRP < 6mg/dl	0	12	12
Total	39	20	59



Sensitivity -82.9%

Specificity – 100%

Predictive value of positive test -100%

Predictive value of negative test – 60%

Accuracy – 66.6%  
The result of  $p = 0.3308 > 0.025$  (Z test for difference of proportions).

In the study population of 75, 78% (59) patients CRP and WBC count in combination was either raised (66%) or normal (34%). None of the HPE negative patients had a raised CRP & WBC combined. None of the HPE negative cases had raised CRP and WBC count in combination.

## VI. DISCUSSION

In the study period from July 2018– July 2020, around 200 cases were operated for appendicitis in this institution i.e, HI-TECH Medical College Hospital and Hospital,Bhubaneswar. Patients who came for interval appendicectomy and patients with conditions raising CRP values were excluded from the study. 75 patients who fulfilled the criteria and operated for suspected acute appendicitis were taken into this study.

Out of 75 patients, 25(33%) were females and 50(67%) were males. So male predominance is there in this study. Appendicitis is common in age groups 20-29 years and 10-19 years in this study. Appendicitis reaches peak incidence in the teens and early 20's<sup>5</sup>.

Clinical diagnosis was found to be correct in 84% of cases and negative appendicectomy rate was 16% in this study. This is comparable with the study done by Erikson<sup>19</sup> (14%) and Gurleyik (16%)<sup>20,4</sup>.

Out of 12 patients who were HPE

negative, 7(58%) were females and 5(42%) were males.

In the study done by Goroos Group A (100)-62% female and 38% male patients had negative appendicectomy<sup>21</sup>.

The diagnostic accuracy of acute appendicitis in women of child bearing age was low because so many other conditions mimic appendicitis<sup>21</sup>. So, laparoscopy can be used as a diagnostic tool particularly in women of child bearing age<sup>1,21</sup>.

The sensitivity and specificity of CRP in case of acute appendicitis were 73% and 100% respectively in this study. This is comparable to the results of study done by Asafar<sup>22</sup> where sensitivity and specificity were 86.6% and 93.6% respectively. This is also supported by studies done by Shakhartreh<sup>23</sup> and Peltola<sup>9</sup>.

In this study, none of the cases with appendicular perforation or abscess formation had normal CRP. This observation is supported by the study done by Gronroo's and Gronroo's<sup>21</sup>.

In this study, 27% of cases had normal CRP levels even though HPE was positive. CRP becomes positive if symptoms are present for more than 12 hours. CRP values were found to increase with an advancing stage of the appendiceal inflammation found at operation and the length of preoperative phase of illness.

Erikson<sup>17</sup> in his study concluded that repeated laboratory tests for CRP and WBC count should be performed in patients with suspected acute appendicitis requested to stay for further observation.

In this study, all the 12 cases which were HPE negative had normal CRP levels. So it was advised by Thimsen<sup>11</sup> in his study that if the



symptoms are present for more than 12 hours and CRP was negative, acute appendicitis was unlikely. It is better to follow these patients in an out patient setting and do repeated clinical examination and repeat investigations. So the negative appendectomy rates can be reduced. In this study CRP and acute appendicitis were highly associated ( $p=0.04923 > 0.025$ )

On correlating TLC with HPE positive and negative cases it was found that the sensitivity and specificity of the WBC count was 76% and 100%. It was comparable with the studies done by Hoffmann<sup>6</sup> (81-84%) Peltola<sup>9</sup> (76%) Marchand<sup>7</sup> (81-84%) Yang<sup>25</sup> (71.4%) indicating high association between WBC count and acute appendicitis ( $p=0.011439 > 0.025$ )

In this study, Neutrophilia of more than 75% was seen in 76% of cases. It is comparable with other studies done by Verma<sup>18</sup> (75%), Hoffman<sup>6</sup> (78%), Marchand<sup>7</sup> (81%) and Yang<sup>25</sup> (88%). In 8% of cases even though there was no raise in WBC count, neutrophil count was raised. None of the cases with HPE negative report had raise in neutrophil count. This indicates that there was high association between raised neutrophil counts and acute appendicitis. ( $p=0.11439 > 0.025$ )

In this study we correlated the total leucocyte count and CRP in combination with histopathologically positive and negative cases. The sensitivity and specificity is 82% and 100%. None of the cases with HPE negative results had increase in CRP, WBC count or neutrophilia. Same observations were found by Nordback<sup>10</sup>, Van Diejen-Visser<sup>15</sup>, Peltola<sup>9</sup>, Merchand<sup>7</sup>, Yang<sup>25</sup>, Ducholm<sup>12</sup>.

When combined value of CRP, WBC and raised neutrophil count is taken into consideration negative value was important. Avoiding surgery in these cases can reduce negative appendectomy rate considerably. ( $p=0.3308 > 0.025$ ).

## VII. CONCLUSIONS

- 1) CRP, TLC & raised neutrophil count are useful in the diagnosis of acute appendicitis.
- 2) Negative appendectomy rate can be decreased, if appendectomy is avoided in cases where all three tests are negative.
- 3) Diagnostic laparoscopy is advised in case of females with suspected appendicitis.

## SUMMARY

75 cases of suspected acute appendicitis operated in Hi-Tech Medical College and Hospital were taken for study. The diagnostic accuracy, sensitivity and specificity of CRP and leucocyte count in diagnosing acute appendicitis was

evaluated.

- Out of 75 cases, 25 were females and 50 were males.
- Age group ranged from 6 to 65 years.
- Maximum group of patients belonged to 20 to 29 years (28%) and 10 to 19 years (20%).
- Clinical diagnosis was correct in 84% of cases.
- Negative appendectomy rate was 16%.
- Negative appendectomy rate was high in females (58%).
- None of the 12 cases (16%) where HPE was negative, had raise in CRP or TLC or neutrophil count.
- All the 17 cases (23%) with perforation or abscess formation had positive CRP test.
- CRP was raised in 73% of HPE positive cases
- WBC was raised in 76% of HPE positive cases
- Neutrophilia was present in 76% of HPE positive cases. 8% of cases had neutrophilia even though WBC count was normal.
- None of the cases had rise in combined value where HPE was negative.
- Negative appendectomy rate can be decreased if appendectomy is avoided in cases where all the three test were negative
- P value was significant in all 3 tests.

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