IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 2 Ser.4 (February. 2022), PP 19-27
www.iosrjournals.org

A Prospective Comparitive Study of Diagnostic Accuracy of C-Reactive Protein, Leucocyte Count And Procalcitonin For Suspected Acute Appendicitis.

DR.S.LALEETHAMBIGA M.S.
Assistant Surgeon, General Surgery, Government Hospital Komarapalayam,Namakkal DT.

DR.T.MANIKANDAN M.S.
DLO., Associate Professor, Department of General Surgery, Government Namakkal Medical College And Hospital,Namakkal.
CORRESPONDING AUTHOR: DR.T.MANIKANDAN M.S.,DLO.,

Abstract
Background
Studies show that CRP, Procalcitonin and Leucocyte count are not sensitive tools for diagnosis. Out of the three biomarkers, CRP has the best discriminative capacity in the diagnosis of acute appendicitis. This is followed by leucocyte count and Procalcitonin. All of them had poor sensitivity and a negative likelihood ratio.
Aim and Objective
The aim was to evaluate the diagnostic value of Procalcitonin, C –reactive protein and Leucocyte count in uncomplicated or complicated appendicitis
Material and Methods
From October 2018 to October 2020, a prospective comparative studywas done 50 patients with clinical diagnosis of acute appendicitis. CRP, Procalcitonin and Total count were recorded. The data was then cleaned, checked for inconsistencies, missing values and prepared for analysis using SPSS v23. The tests for significance were run to statistically validate the data. Mann-Whitney U test was done. A ROC analysis along with the AUC was performed to understand the sensitivity and specificity of the biomarkers.
Results
The mean CRP level is 51.1 mg/dl with a standard deviation of 36.43 mg/dl. The mean total count is 10479.4 cells/cu.mm with a standard deviation of 5509.8 cells/cu.mm. The mean Procalcitonin level is 8.77 ng/ml with a standard deviation of 7.13 ng/ml.Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and CRP values. Complicated appendicitis have higher CRP values. Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and total count. Complicated appendicitis have higher total count. Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and Procalcitonin values. Complicated appendicitis have higher Procalcitonin values.Larger values of the test result variable(s) indicate stronger evidence for a positive actual state. This means that higher values of CRP, Procalcitonin and Total Count indicate complication. This association is statistically significant ($p<0.005$). However, ROC curve and area under the curve shows that sensitivity is low and can be non-specific too. CRP(mg/dl), TC(cells/cu.mm), PCT(ng/ml) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.
Conclusion
Procalcitonin has little value in diagnosing acute appendicitis with lower diagnostic accuracy than CRP and leucocyte count. However, Procalcitonin has greater diagnostic value in identifying complicated appendicitis.

Date of Submission: 26-01-2022 Date of Acceptance: 07-02-2022

I. Introduction

Acute appendicitis is one of the most common conditions accounting for a substantial number of emergency hospital admissions[1]. Although it can present in any age, it has a higher preponderance in the younger age group between 10 and 20 years[2]. Males are 1.4 times more affected than females with an estimated lifetime risk of 8.6% for males and 6.7% for females. It leads to loss of number of days in hospital and costs billions annually for the patients and the insurers[3].The diagnosis is done clinically as most of the patients present with a typical history and clinical presentation. The etiology of acute appendicitis is largely unknown though

dietary and intraluminal factors have been implicated in this[4]. Management is always surgical removal of the appendix (appendicectomy). Earlier it was predominantly an open surgical procedure. Nowadays, it is more of a laparoscopic procedure. There are also cases of negative appendicectomy (around 10%) due to a similar presentation by other inguino-pelvic disorders[5-7].

Newer imaging modalities like CT have been used to reduce the false positivity rates. However, exposure to radiation, cost of equipment, manpower and maintenance discourages widespread use of such imaging techniques[8-10]. Also, delay in diagnosis may lead to systemic complications like sepsis and ruptured appendicitis.This is why there is a need for finding, validating and using biomarkers that can be easily measured, easy to detect, simple and sensitive. Also, the hassles of setting up and maintaining an imaging infrastructure are more costly than using simple laboratory tests.Conventional white blood cell count is non-specific. It is neither sensitive. Any pain in the right lower abdominal quadrant sees an increase in white blood cell count by around 70%[11]. C-reactive protein is more specific than leucocyte though it is less sensitive in the early stages of acute appendicitis[12,13]. Also, CRP is more sensitive in detecting complicated appendicitis. Therefore, using CRP and WBC together might improve the diagnostic accuracy of the clinical decisions.Recent studies focus on the role of Procalcitonin in the diagnosis of acute appendicitis[16-21]. Procalcitonin is the precursor of calcitonin which is secreted by the C cells of the thyroid gland and K cells of the lung. In healthy individuals, Procalcitonin is undetectable (<0.05 ng/ml). However, when these cells are stimulated by endotoxins and inflammatory cytokines, Procalcitonin is released from the parenchymal tissues throughout the body[22-24]. One of the reasons why Procalcitonin is superior to CRP is that it doesn't increase in response to viral infection or sterile inflammation.Studies show that CRP, Procalcitonin and leucocyte count are not sensitive tools for diagnosis[26]. There is a high positive likelihood ratio for CRP and a high diagnostic accuracy for Procalcitonin for complicated appendicitis. If these tests are suggestive of acute appendicitis, then more advanced imaging studies can be done to rule out other causes. This is important to make a clinical decision whether to manage the case surgically or medically. Also, biomarkers can be used for follow-up.Out of the three biomarkers, CRP has the best discriminative capacity in the diagnosis of acute appendicitis. This is followed by leucocyte count and Procalcitonin. All of them had poor sensitivity and a negative likelihood ratio.The reason why CRP is superior to Procalcitonin can be explained by the wide etiology of acute appendicitis[27]. Infectious etiology has a different biomarker presentation while non-infectious etiology is caused by the obstruction of the lumen thereby leading to local inflammation[28]. Secondary bacterial infection may lead to an increase in Procalcitonin levels and thereby prove as an better diagnostic aid. CRP is more accurate in the diagnosis of perforated appendicitis than overall acute appendicitis. However, metaanalyses show that Procalcitonin is better in diagnosing complicated acute appendicitis.Therefore the use of biomarkers will help in making clinical decisions regarding the use of antibiotics and performing surgery. Also, it can be used as a follow-up.

Aim of the Study

The aim was to evaluate the diagnostic value of Procalcitonin, C - reactive protein and Leucocyte count in uncomplicated or complicated appendicitis.

Objectives of the study

Primary Objective

The aim was to evaluate the diagnostic value of Procalcitonin, C - reactive protein and Leucocyte count in uncomplicated or complicated appendicitis

Secondary Objective

To study the clinical profile of patients getting admitted with acute appendicitis

To compare the various sociodemographic, clinical and laboratory parameters between complicated and uncomplicated appendicitis

To compare the diagnostic accuracy of the biomarkers in the study**MATERIALS AND METHODS**

STUDY DESIGN

A Prospective Comparative study

STUDY POPULATION

This study includes 50 patients with clinical diagnosis of acute appendicitis

STUDY PERIOD

From OCTOBER 2018 TO OCTOBER 2020

SAMPLE SIZE

This study includes 50 patients with clinical diagnosis of acute appendicitis

INCLUSION CRITERIA

All the patients admitted to general surgical ward with clinical diagnosis of acute appendicitis

EXCLUSION CRITERIA

Infants

II. Methodology

The material for the study is taken from the cases admitted to department of General Surgery in GMK Medical College & Hospital Salem, who are clinically diagnosed to have acute appendicitis.

a) A detailed history is taken and examination is done to diagnose acute appendicitis.
b) Clinical evaluation was done
c) Laboratory investigations were done
d) CRP, Procalcitonin and Total count were recorded
e) Patients were followed up till their discharge and at periodic intervals.

PRIVACY/CONFIDENTIALITY OF STUDY SUBJECTS:

Privacy of the subjects shall be maintained.

STATISTICAL ANALYSIS

All data were recorded in structured questionnaires, coded and entered in Microsoft Excel. The data was then cleaned, checked for inconsistencies, missing values and prepared for analysis using SPSS v23. The data was then analyzed for descriptive statistics and inferential statistics. The tests for significance were run to statistically validate the data. Mann-Whitney U-test and Chi-square analyses were done. A ROC analysis along with the AUC was performed to understand the sensitivity and specificity of the biomarkers. The results were then tabulated and visualized in Microsoft word.

III. Results

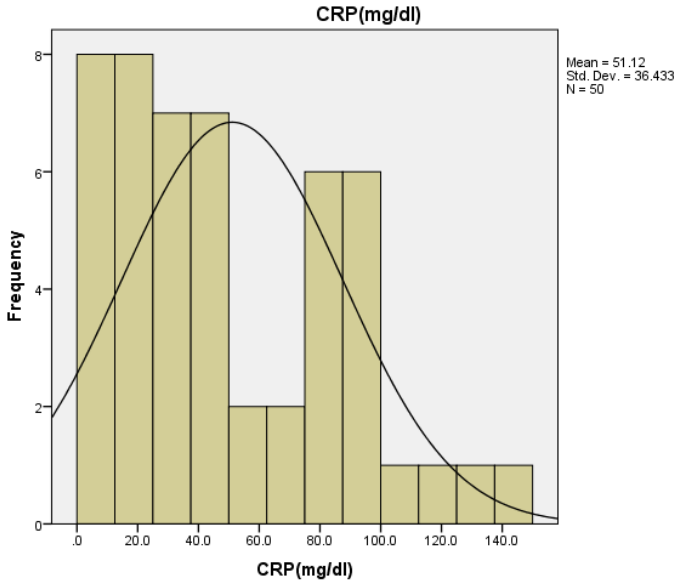
The aim was to evaluate the diagnostic value of Procalcitonin, C - reactive protein and Leucocyte count in uncomplicated or complicated appendicitis. This research also aimed to study the clinical profile of patients getting admitted with acute appendicitis, to compare the various sociodemographic, clinical and laboratory parameters between complicated and uncomplicated appendicitis and to compare the diagnostic accuracy of the biomarkers in the study.The study revealed the following findings.Around 66% (n=33) of them had uncomplicated appendicitis while 34% (n=17) had complicated appendicitis.The mean CRP level is 51.1 mg/dl with a standard deviation of 36.43 mg/dl. It ranges between 2-144 mg/dl. The median CRP level is 43.5 mg/dl.The mean total count is 10479.4 cells/cu.mm with a standard deviation of 5509.8 cells/cu.mm. It ranges between 3400-22000 cells/cu.mm days. The median total count is 8200 cells/cu.mm days.The mean Procalcitonin level is 8.77 ng/ml with a standard deviation of 7.13 ng/ml. It ranges between 1-34 ng/ml. The median level is 7 ng/ml.

Important parameters were compared between complicated and uncomplicated appendicitis. Mann-Whitney U test was performed and p-value <0.05 was considered statistically significant.

Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and CRP values. Complicated appendicitis have higher CRP values.Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and total count. Complicated appendicitis have higher total count. Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and Procalcitonin values. Complicated appendicitis have higher Procalcitonin values.Larger values of the test result variable(s) indicate stronger evidence for a positive actual state. This means that higher values of CRP, Procalcitonin and Total Count indicate complication. This association is statistically significant ($p<0.005$). However, ROC curve and area under the curve shows that sensitivity is low and can be non-specific too. CRP(mg/dl), TC(cells/cu.mm), PCT(ng/ml) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. This was done under the non-parametric assumption. Procalcitonin has little value in diagnosing acute appendicitis with lower diagnostic accuracy than CRP and leucocyte count. However, Procalcitonin has greater diagnostic value in identifying complicated appendicitis.

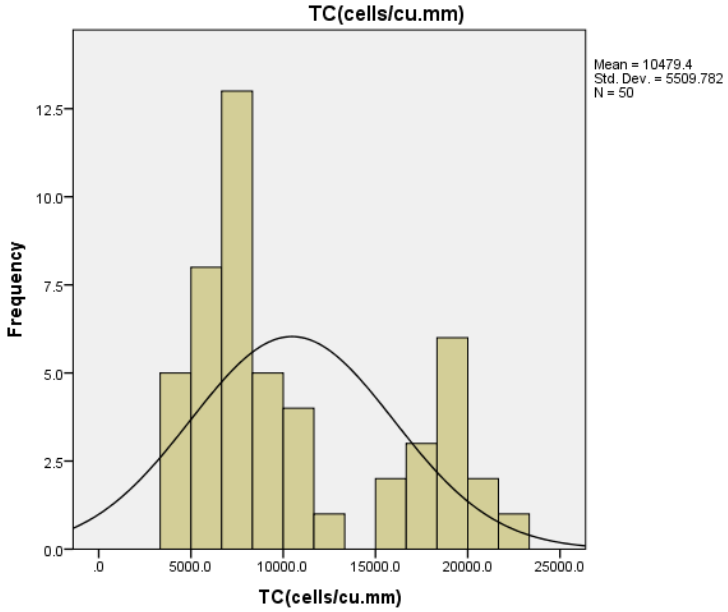
CRP levels

The mean CRP level is 51.1 mg/dl with a standard deviation of 36.43 mg/dl. It ranges between 2-144 mg/dl. The median CRP level is 43.5 mg/dl.



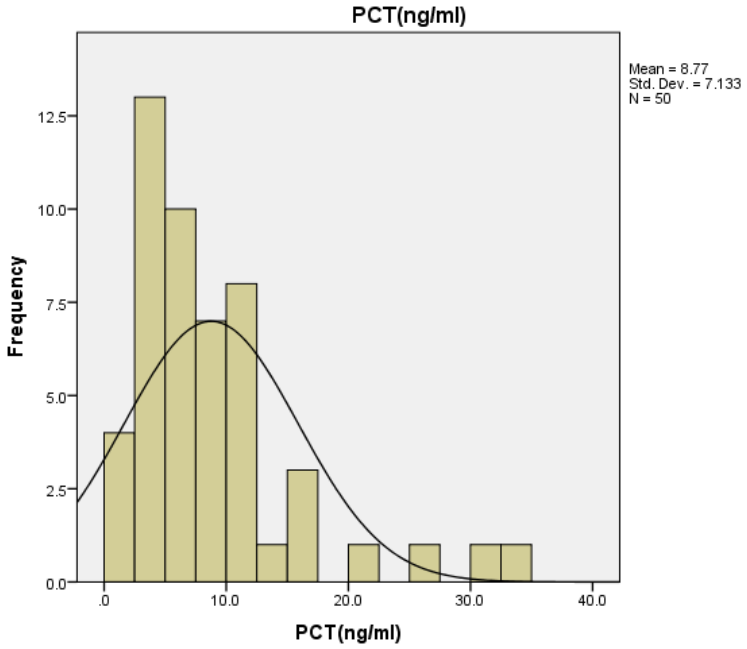
Total Count

The mean total count is 10479.4 cells/cu.mm with a standard deviation of 5509.8 cells/cu.mm. It ranges between 3400-22000 cells/cu.mm days. The median total count is 8200 cells/cu.mm days.



Procalcitonin

The mean Procalcitonin level is 8.77 ng/ml with a standard deviation of 7.13 ng/ml. It ranges between 1-34 ng/ml. The median level is 7 ng/ml.



Inferential statistics

Important parameters were compared between complicated and uncomplicated appendicitis. Mann-Whitney U test was performed and p-value <0.05 was considered statistically significant. The following tables shows the findings from the analysis.

Relationship between diagnosis and CRP

Mann-Whitney U test shows that there is significant relationship (p<0.005) between the complication of appendicitis and CRP values. Complicated appendicitis have higher CRP values.

	DIAGNOSIS	N	Mean Rank	Sum of Ranks
CRP(mg/dl)	Uncomplicated appendicitis	33	18.42	608.00
	Complicated appendicitis	17	39.24	667.00
	Total	50		

Relationship between diagnosis and CRP levels

	CRP(mg/dl)
Mann-Whitney U	47.000
Wilcoxon W	608.000
Z	-4.785
Asymp. Sig. (2-tailed)	.000

Relationship between diagnosis and Total Count

Mann-Whitney U test shows that there is significant relationship (p<0.005) between the complication of appendicitis and total count. Complicated appendicitis have higher total count.

	DIAGNOSIS	N	Mean Rank	Sum of Ranks
TC(cells/cu.mm)	Uncomplicated appendicitis	33	17.71	584.50
	Complicated appendicitis	17	40.62	690.50
	Total	50		

Relationship between diagnosis and total count

	TC(cells/cu.mm)
Mann-Whitney U	23.500
Wilcoxon W	584.500
Z	-5.265
Asymp. Sig. (2-tailed)	.000

Relationship between diagnosis and Procalcitonin levels

Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and Procalcitonin values. Complicated appendicitis have higher Procalcitonin values.

	DIAGNOSIS	N	Mean Rank	Sum of Ranks
PCT(ng/ml)	Uncomplicated appendicitis	33	18.88	623.00
	Complicated appendicitis	17	38.35	652.00
	Total	50		

Relationship between diagnosis and Procalcitonin levels

	PCT(ng/ml)
Mann-Whitney U	62.000
Wilcoxon W	623.000
Z	-4.480
Asymp. Sig. (2-tailed)	.000

ROC Analysis

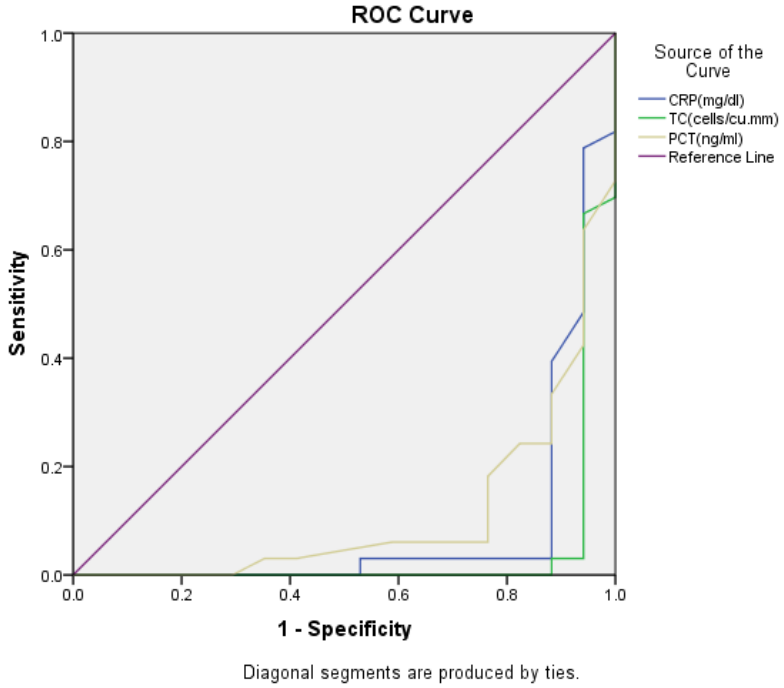
The following section shows the ROC analysis. **Larger values of the test result variable(s)** indicate stronger evidence for a positive actual state. This means that higher values of CRP, Procalcitonin and Total Count indicate complication. This association is statistically significant ($p<0.005$). However, ROC curve and area under the curve shows that sensitivity is low and can be non-specific too. CRP(mg/dl), TC(cells/cu.mm), PCT(ng/ml) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. This was done under the non-parametric assumption. Procalcitonin has little value in diagnosing acute appendicitis with lower diagnostic accuracy than CRP and leucocyte count. However , Procalcitonin has greater diagnostic value in identifying complicated appendicitis.

Case Processing Summary	
DIAGNOSIS	Valid N (listwise)
Positive[a]	33
Negative	17
Larger values of the test result variable(s) indicate stronger evidence for a positive actual state.	
a. The positive actual state is 1.0.	

ROC analysis

Area Under the Curve					
Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
CRP(mg/dl)	.084	.052	.000	.000	.187
TC(cells/cu.mm)	.042	.040	.000	.000	.119
PCT(ng/ml)	.111	.050	.000	.012	.209
The test result variable(s): CRP(mg/dl), TC(cells/cu.mm), PCT(ng/ml) 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					

AUC



ROC Curve

IV. Discussion

The study revealed the following findings: The mean CRP level is 51.1 mg/dl with a standard deviation of 36.43 mg/dl. It ranges between 2-144 mg/dl. The median CRP level is 43.5 mg/dl.The mean total count is 10479.4 cells/cu.mm with a standard deviation of 5509.8 cells/cu.mm. It ranges between 3400-22000 cells/cu.mm days. The median total count is 8200 cells/cu.mm days.The mean Procalcitonin level is 8.77 ng/ml with a standard deviation of 7.13 ng/ml. It ranges between 1-34 ng/ml. The median level is 7 ng/ml.

Important parameters were compared between complicated and uncomplicated appendicitis.Mann-Whitney U test was performed and p-value <0.05 was considered statistically significant.Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and CRP values. Complicated appendicitis have higher CRP values.Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and total count. Complicated appendicitis have higher total count. Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and Procalcitonin values. Complicated appendicitis have higher Procalcitonin values.Larger values of the test result variable(s) indicate stronger evidence for a positive actual state. This means that higher values of CRP, Procalcitonin and Total Count indicate complication. This association is statistically significant ($p<0.005$). However, ROC curve and area under the curve shows that sensitivity is low and can be non-specific too. CRP(mg/dl), TC(cells/cu.mm), PCT(ng/ml) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. This was done under the non-parametric assumption. Procalcitonin has little value in diagnosing acute appendicitis with lower diagnostic accuracy than CRP and leucocyte count. However, Procalcitonin has greater diagnostic value in identifying complicated appendicitis.

Conventional white blood cell count is non-specific. It is neither sensitive. Any pain in the right lower abdominal quadrant sees an increase in white blood cell count by around 70%[11]. C-reactive protein is more specific than leucocyte though it is less sensitive in the early stages of acute appendicitis[12,13]. Also, CRP is more sensitive in detecting complicated appendicitis. Therefore, using CRP and WBC together might improve the diagnostic accuracy of the clinical decisions.Recent studies focus on the role of Procalcitonin in the diagnosis of acute appendicitis. Procalcitonin is the precursor of calcitonin which is secreted by the C cells of the thyroid gland and K cells of the lung. In healthy individuals, Procalcitonin is undetectable (<0.05 ng/ml). However, when these cells are stimulated by endotoxins and inflammatory cytokines, Procalcitonin is released from the parenchymal tissues throughout the body[22-24]. One of the reasons why Procalcitonin is superior to CRP is that it doesn't increase in response to viral infection or sterile inflammation.Studies show that CRP, Procalcitonin and leucocyte count are not sensitive tools for diagnosis. There is a high positive likelihood ratio for CRP and a high diagnostic accuracy for Procalcitonin for complicated appendicitis. If these tests are suggestive of acute

appendicitis, then more advanced imaging studies can be done to rule out other causes. This is important to make a clinical decision whether to manage the case surgically or medically. Also, biomarkers can be used for follow-up.

Out of the three biomarkers, CRP has the best discriminative capacity in the diagnosis of acute appendicitis. This is followed by leucocyte count and Procalcitonin. All of them had poor sensitivity and a negative likelihood ratio.The reason why CRP is superior to Procalcitonin can be explained by the wide etiology of acute appendicitis[27]. Infectious etiology has a different biomarker presentation while non-infectious etiology is caused by the obstruction of the lumen thereby leading to local inflammation[28]. Secondary bacterial infection may lead to an increase in Procalcitonin levels and thereby prove as an better diagnostic aid. CRP is more accurate in the diagnosis of perforated appendicitis than overall acute appendicitis. However, metaanalyses show that Procalcitonin is better in diagnosing complicated acute appendicitis.

Therefore the use of biomarkers will help in making clinical decisions regarding the use of antibiotics and performing surgery. Also, it can be used as a follow-up. Procalcitonin has little value in diagnosing acute appendicitis with lower diagnostic accuracy than CRP and leucocyte count. However, Procalcitonin has greater diagnostic value in identifying complicated appendicitis.

V. Conclusions

The aim was to evaluate the diagnostic value of Procalcitonin, C - reactive protein and Leucocyte count in uncomplicated or complicated appendicitis. This research also aimed to study the clinical profile of patients getting admitted with acute appendicitis, to compare the various sociodemographic, clinical and laboratory parameters between complicated and uncomplicated appendicitis and to compare the diagnostic accuracy of the biomarkers in the study. The study revealed the following findings;Around 66% (n=33) of them had uncomplicated appendicitis while 34% (n=17) had complicated appendicitis.Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and CRP values. Complicated appendicitis have higher CRP values. Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and total count. Complicated appendicitis have higher total count. Mann-Whitney U test shows that there is significant relationship ($p<0.005$) between the complication of appendicitis and Procalcitonin values. Complicated appendicitis have higher Procalcitonin values.Cross tabulation and chi-square analysis between diagnosis and fever showed that there is a significant relationship between fever and diagnosis ($p<0.05$). Larger values of the test result variable(s) indicate stronger evidence for a positive actual state. This means that higher values of CRP, Procalcitonin and Total Count indicate complication. This association is statistically significant ($p<0.005$). However, ROC curve and area under the curve shows that sensitivity is low and can be non-specific too. CRP(mg/dl), TC(cells/cu.mm), PCT(ng/ml) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. This was done under the non-parametric assumption. Procalcitonin has little value in diagnosing acute appendicitis with lower diagnostic accuracy than CRP and leucocyte count. However, Procalcitonin has greater diagnostic value in identifying complicated appendicitis.

References

[1]. Hospital Episode Statistics. Primary diagnosis: summary. www.hesonline.nhs.uk/Ease/servlet/ ContentServer?siteID = 1937&categoryID = 202

[2]. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol 1990;132:910-25.

[3]. Davies GM, Dasbach EJ, Teutsch S. The burden of appendicitis-related hospitalizations in the United States in 1997. *Surg Infect (Larchmt)* 2004; **5**: 160–165.

[4]. Larner AJ. The aetiology of appendicitis. Br J Hosp Med 1988;39:540-2

[5]. Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. *Arch Surg* 2002; **137**: 799–804.

[6]. Flum DR, Morris A, Koepsell T, Dellinger EP. Has misdiagnosis of appendicitis decreased over time? A population-based analysis. *JAMA* 2001; **286**: 1748–1753.

[7]. Graff L, Russell J, Seashore J, Tate J, Elwell A, Prete M *et al*.False-negative and false-positive errors in abdominal pain evaluation: failure to diagnose acute appendicitis and unnecessary surgery. *Acad Emerg Med* 2000; **7**: 1244–1255.

[8]. Doria AS, Moineddin R, Kellenberger CJ, Epelman M, Beyene J, Schuh S *et al*. US or CT for diagnosis of

[9]. appendicitis in children and adults? A meta-analysis. *Radiology* 2006; **241**: 83–94.

[10]. Hlibczuk V, Dattaro JA, Jin Z, Falzon L, Brown MD. Diagnostic accuracy of noncontrast computed tomography

[11]. for appendicitis in adults: a systematic review. *Ann Emerg Med* 2010; **55**: 51–59.e1.

[12]. Obermaier R, Benz S, Asgharnia M, Kirchner R, Hopt UT. Value of ultrasound in the diagnosis of acute appendicitis: interesting aspects. *Eur J Med Res* 2003; **8**: 451–456.

[13]. Andersson RE. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. *Br J Surg* 2004; **91**: 28–37.

[14]. Wen SW, Naylor CD. Diagnostic accuracy and short-term surgical outcomes in cases of suspected acute appendicitis. *CMAJ* 1995; **152**: 1617–1626.

[15]. Torcivia A, Vons C, Barrat C, Dufour F, Champault G. Influence of mesh type on the quality of early outcomes after inguinal hernia repair in ambulatory setting controlled study: Glucamesh□□*vs* Polypropylene□. *angenbecks Arch Surg* 2011; **396**: 173–178.

[16]. Sack U, Biereder B, Elouahidi T, Bauer K, Keller T, Trobs RB. Diagnostic value of blood inflammatory markers

[17]. for detection of acute appendicitis in children. *BMC Surg* 2006; **6**: 15.
[18]. Stefanutti G, Ghirardo V, Gamba P. Inflammatory markers for acute appendicitis in children: are they helpful? *J Pediatr Surg* 2007; **42**: 773–776.

DR.S.LALEETHAMBIGA M.S., et. al. "A Prospective Comparitive Study of Diagnostic Accuracy of C-Reactive Protein, Leucocyte Count And Procalcitonin For Suspected Acute Appendicitis." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(02), 2022, pp. 19-27.