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Efficacy of the serum Procalcitonin in predicting complicated appendicitis: A study of 110 cases of acute appendicitis

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Abstract
Background- *Delay in the diagnosis of complicated appendicitis and its treatment results in an increased rate of postoperative morbidity, mortality and hospital stay. The diagnosis of appendicitis rests on a combination of signs of inflammation such as fever, pain & tenderness; leukocytosis, and elevated C-reactive protein levels, interleukin- 6 (IL6) and Procalcitonin . In the absence of signs of inflammation the diagnosis is less certain, and in this situation an imaging CT scan may be of value. Raised level of serum procalcitonin in bacterial infection has been used to further improve the diagnosis of complicated AA. The aim of this study was to assess the value of procalcitonin as a predictor of severity of appendicitis in order to make the clinical decision for intervention*
Methods - *One-hundred ten patients of appendicitis confirmed by intra-operative findings & final pathologist report, who underwent appendectomy consisting 25 women (22.73%) and 85 men (77.27%) with a mean age of 25 years (age range 15-55 years) were included in this study. Serum Procalcitonin value was measured by chemi E411 Cobas method (chemilumiscent immunoassay system) using the B.R.A.H.M.S PCT kit. Serum PCT level >0.5ng/mL was consider as risk for progression to severe systemic disease.*
Results- *At a 0.5 ng/dl cut-off value of PCT, the sensitivity and specificity of PCT level measurement for acute complicated appendicitis prediction was 90% and 97.14% respectively. The PPV and NPV of PCT in complicated appendicitis were (94.74%) and (94.44%) respectively.*
Conclusions- *The PCT values can be used as predictor of complicated appendicitis & infectious complications following surgery for acute appendicitis and it can help to carry out timely surgical intervention which is highly recommended in patients with values more than 0.5ng/ml & also in this high litigation era, it can guide you to explain the incidence of possible surgical site complications in complicated appendicitis to the patients & its attendants.*
Keywords – *complicated acute appendicitis/ AA , procalcitonin*

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I. Introduction

It is estimated that as much as 6% to 7% of the general population will develop appendicitis during their lifetime, with the incidence peaking in the second decade of life[1].

As appendicitis progresses, the blood supply is impaired by bacterial infection in the wall and distention of the lumen; gangrene and perforation occurs at about 24 hours, though the timing is highly variable. Gangrene implies microscopic perforation, bacterial contamination of the peritoneum, and peritonitis. This process may be effectively localized by adhesions from nearby viscera[2].

Appendectomy remains one of the most commonly performed operations worldwide[3].

The clinical diagnosis of appendicitis rests on a combination of localized pain and tenderness accompanied by signs of inflammation, such as fever, leukocytosis, and elevated C-reactive protein levels. In the absence of signs of inflammation the diagnosis is less certain, and in this situation a CT scan may be of value[2].

Following the introduction and widespread use of antibiotics in the 1940s, mortality rates improved further. C-reactive protein, bilirubin, Il-6, and procalcitonin have all been suggested to be helpful in the diagnosis of appendicitis, specifically in predicting perforated appendicitis[4].

Delay in diagnosis and treatment results in an increased rate of perforation, postoperative morbidity, mortality and hospital stay.

The aim of this study was to assess the value of procalcitonin[5,6] as a predictor of severity of appendicitis in order to improve the clinical decision making.

Aims & Objectives

Aims - To study efficacy of serum procalcitonin in predicting complicated appendicitis

Objective

1. ***Primary objective***- To assess the value of procalcitonin as a predictor of severity (inflamed, gangrenous, perforated) of appendicitis in order to improve the clinical decision making for timely intervention.
2. ***Secondary objective*** - To establish relation between histopathological finding of appendix & its correlation with post operative complications.

II. Materials & Methods

Study design was Hospital based cross sectional study. Study was conducted in between 1st January, 2018 to 31st November , 2019.Study area was Department of general surgery of SMS hospital, SMS medical college, Jaipur.

Study population was selected as per the inclusion and exclusion criteria. Inclusion criteria including those patients who have given written and informed consent, Age group 15-50 years in either sex, All patients without exclusion criteria, who underwent appendectomy, in which peri-operatively complicated appendicitis were found. While Exclusion criteria include diagnosis other than acute appendicitis confirmed during the operation, Presence of another acute infectious lesion or disease in any other part of the body, Immunosuppressive disease like HIV.

Sample size is calculated at 95% confidence level assuming 65% specificity of PCT to detect peritonitis due to appendicitis & prevalence of peritonitis due to appendicitis was 9.5%. At 10% absolute allowable error sample size is found 102 patients of peri-operatively complicated confirmed appendicitis which is further rounded off to 110 such patients.

III. Methodology

Patients diagnosed with symptomatic appendicitis were selected based on the clinical signs or USG report.The patients were informed about the details of the procedure and written informed consent was obtained.Serum Procalcitonin was assessed. And all the cases divided in two groups on the basis of procalcitonin value.Serum Procalcitonin value was measured by chemi E411 Cobas method (chemilumiscent immunoassay system) using the B.R.A.H.M.S PCT kit .Status of the appendix (Peri-operative finding) and histological diagnosis (normal/inflamed/gangrenous/perforated) was recorded. Patients were analyzed whether they have uncomplicated or complicated appendicitis, complicated appendicitis patients were those having gangrenous or perforated appendix with or without appendicular abscess formation. Serum Procalcitonin value <0.5 ng/mL was considered normal. Patients with procalcitonin value >0.5 ng/mL. (value as a risk for progression to severe systemic disease) were consider positive.

Statistical analysis was performed by MS excel worksheet 2007. Analysis of distribution of data was assessed by the Chi-square test.

IV. Results

One-hundred ten patients of appendicitis confirmed by intra-operative findings & final pathologist report, who underwent appendectomy consisted of 25 women (22.73%) and 85 men (77.27%) with a mean age of 25 years (age range 15-55 years) were included in this study.

Mean age was 25 years with standard deviation 31.8. Age group 15-24 yrs & 25-34 yrs have the most common incidence of appendicitis.

Table 1: Age and sex wise distributions of the acute appendicitis case.

AGE /SEX	FEMALE	MALE	TOTAL
15-24	15 (60%)	53(62.35%)	68(61.82%)
25-34	6 (24%)	19(22.35%)	25(22.73%)
35-44	1 (4%)	8(9.41))	9 (8.18%)
45-55	3(12%)	5(5.88%)	8(7.27%)
15-55	25(100%)	85(100%)	110

Female patients having uncomplicated appendicitis were 18 (72%) & complicated in 7 (28%) patients while male patients having uncomplicated appendicitis were 52(61.18%) as compared to complicated appendicitis in 33 (38.82%) patients.

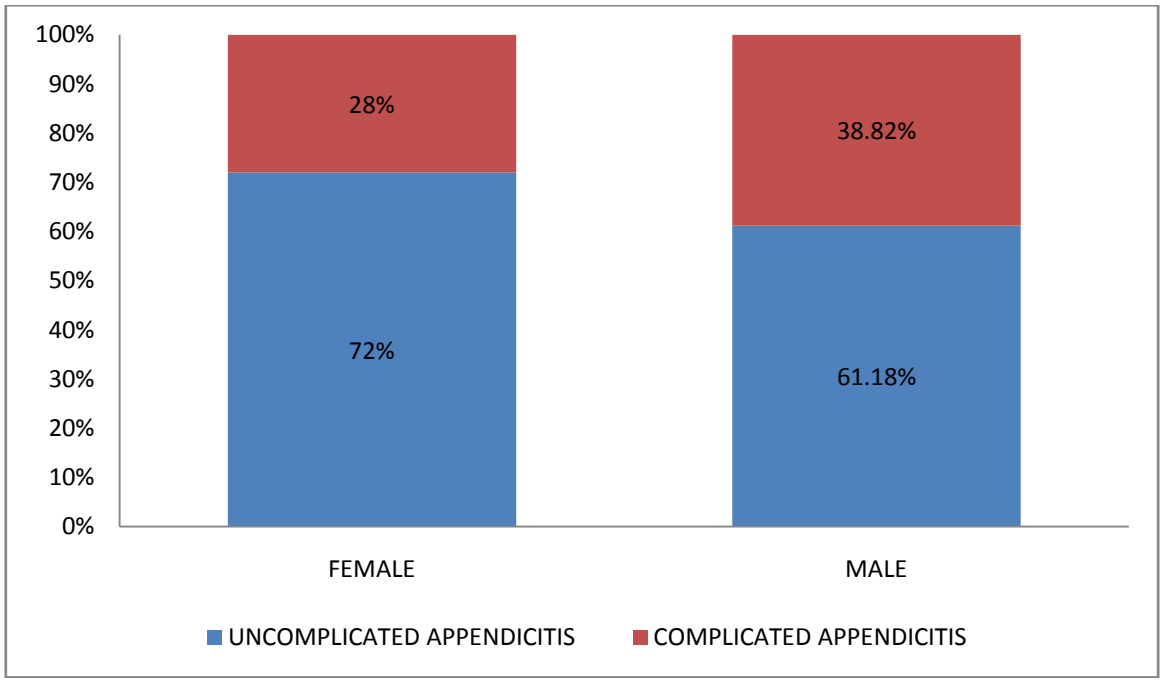
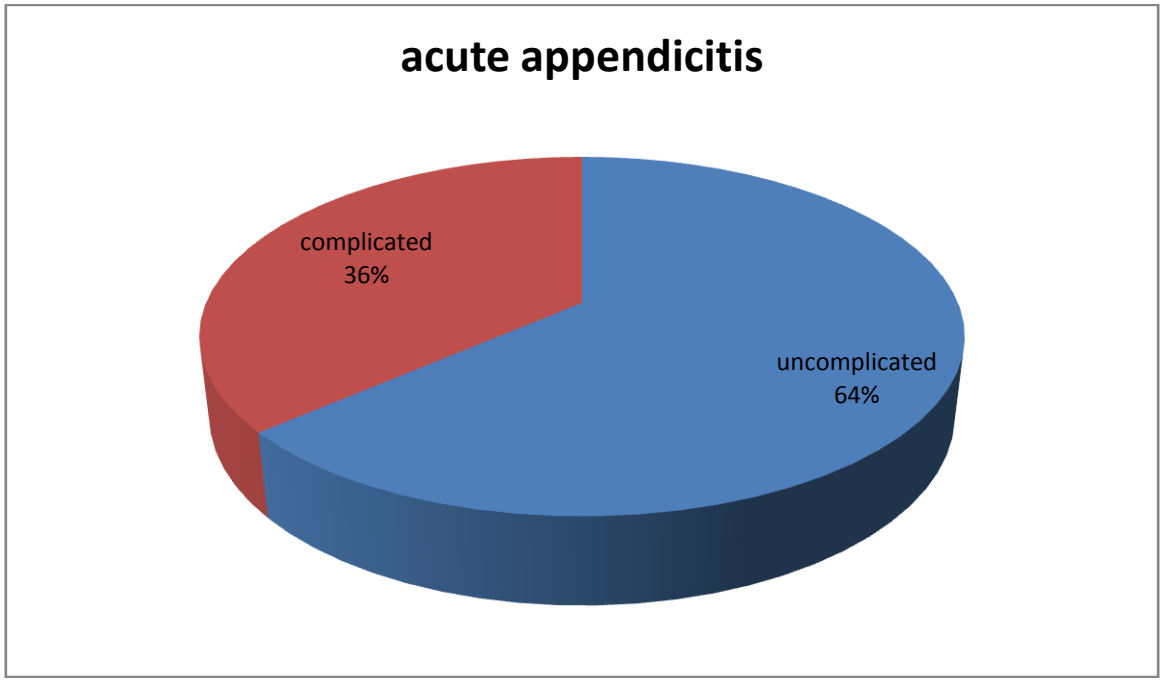


Figure 1: sex wise distribution of complicated and uncomplicated acute appendicitis



Procalcitonin value in 73 patients (26.03% female & 73.97% male patients) was less than 0.5ng/ml and thence considered negative. In the remaining 37 patients (16.22% female & 83.78%male patients), serum PCT value was more than 0.5 ng/ml & these considered positive.

Table 2: sex wise distribution of cutoff level of procalcitonin in acute appendicitis

GENDER/PCT	Uncomplicated AA <0.5	Complicated AA >0.5
FEMALE	19 (26.03%)	6 (16.22%)
MALE	54 (73.97%)	31 (83.78%)
TOTAL	73 (66.36%)	37 (33.64%)

Based on intraoperative finding with the final pathologic report, we classified the patients into two groups: Group I with a complicated appendicitis and Group II with uncomplicated appendicitis.

Table 3: Association of PCT with complicated AA

PCT / AA	COMPLICATED AA	UNCOMPLICATED AA	TOTAL
>0.5	36	2	38
<0.5	4	68	72
	40	70	110

Chi-square =81.676 with 1 degree of freedom; P<0.001 LS=Significant
At a 0.5 ng/dl cut-off value of PCT ,the sensitivity and specificity of PCT level measurement for acute complicated appendicitis prediction was 90% and 97.14% respectively. The PPV and NPV of PCT in complicated appendicitis were (94.74%) and (94.44%) respectively.

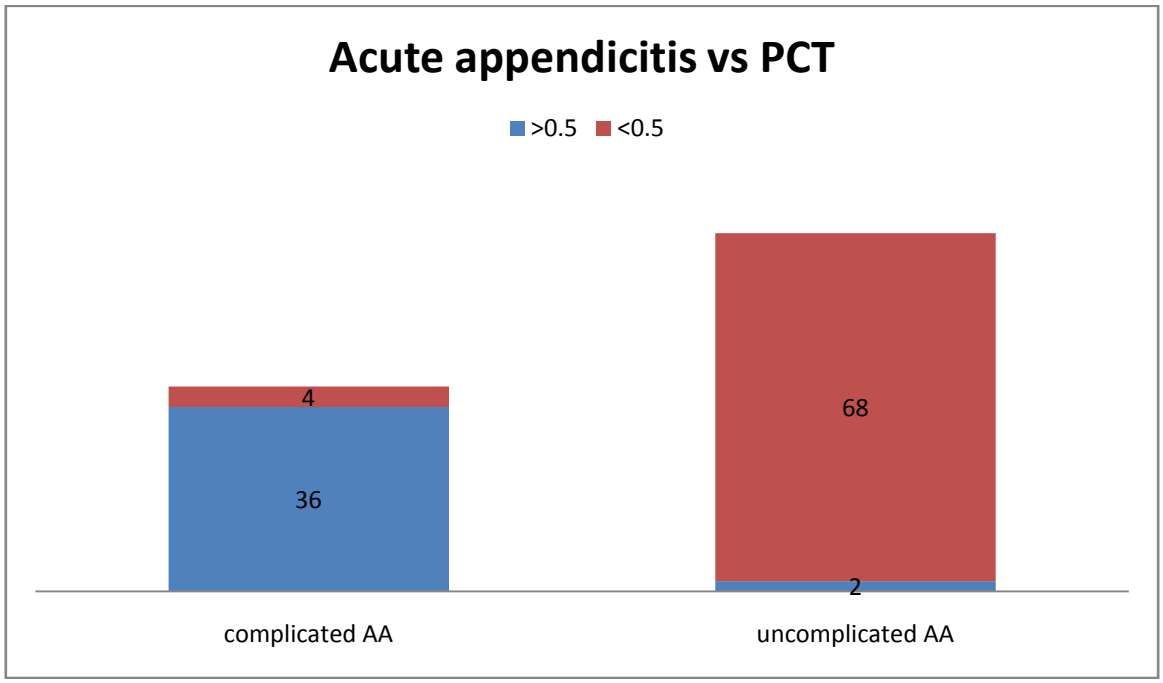


Figure 3: Relation of PCT with Appendicitis

The severity of the appendix inflammation determined for each patient at the time of operation & confirmed by histopathological report known as complicated appendicitis included the following: abscess / gangrenous/perforated appendix (40 patients). Complicated appendicitis may have abscess or perforation (peritonitis) or necrotizing appendicitis which may lead to frequent post operative complication like surgical site infection.

Out of 18 patients with necrotizing appendicitis, 16 (88%) patients had PCT level more than 0.5ng/ml while only 22 (23%) patients out of 92 were having high levels of PCT in uncomplicated appendicitis group.

Peritonitis due to perforated appendicitis was confirmed in 25 patients intra-operatively. Among 25 patients with peritonitis, 21 patients had a PCT value more than 0.5ng/ml .

Post-operative complications including surgical site infection (SSI) was detected in 8 patients. In 8 cases of surgical site infection,7 patient had a PCT value more than 0.5 ng/ml, and one patient had a negative PCT value.

The corresponding sensitivity for detecting peritonitis, necrotizing appendicitis and surgical site infection were 84%,88.89% and 87.5% and their specificity were 80%,76.09% and 69.61% respectively.

V. Discussion

This study included 110 patients with 25 females and 85 males with a mean age of 25 years.

Based on the intra-operative findings (Abscess, gangrenous or perforated appendix), each case was labeled as uncomplicated appendicitis or complicated appendicitis. Peritonitis due to perforated appendicitis was confirmed in 25 patients intra-operatively.

Post-operative complications including surgical site infection (SSI) was detected in 8 patients.

Procalcitonin value in 72 patients was less than 0.5ng/ml and hence considered negative. In the remaining 38 patients, serum PCT value more than 0.5 ng/ml.

Among 25 patients with peritonitis, 21 patients had a PCT value more than 0.5ng/ml . In 8 cases of surgical site infection,7 patient had a PCT value more than 0.5 ng/ml, and one patient had a negative PCT value.

At a 0.5 ng/dl cut-off value of PCT, the sensitivity and specificity of PCT level measurement for acute complicated appendicitis prediction was 90% and 97.14% respectively.

The PPV and NPV of PCT in complicated appendicitis were (94.74%) and (94.44%) respectively

The corresponding sensitivity for detecting peritonitis,necrotizing and surgical site infection were 84%,88.89% and 87.5% and their specificity were 80%,76.09% and 69.61% respectively.

Chandel[7] et al in their study of 40 patients found Sensitivity(95.65%), Specificity(100%) and Predictive values PPV(100%) & NPV(83.3%) of serum PCT levels as the diagnostic test for the diagnosis of acute appendicitis.

Gavela[8] et al study done for diagnosis of peritonitis, a PCT cutoff of 0.18 ng/mL gave a sensitivity of 97%, specificity of 80%, positive predictive value of 72%, and negative predictive value of 89.3%.

Kafetzis[9,10] et al study - There was a statistically significant indication ($p<0.0001$) that PCT levels>0.5 ng/ml are observed more frequently in cases of perforated or necrotizing appendicitis than in simple appendicitis. A PCT level of >0.5 ng/ml can indicate perforation or gangrene with 73% sensitivity and 94% specificity.

In Kouame[11] et al study of 101 children, the sensitivity of PCT was 28%: 95% CI [18–40], 88% specificity: 95% CI [72–97], the predictive value 83% positive: 95% CI [61–95] and predictive value negative 37%: 95% CI [26–49] .The sensitivity does not allow a threshold value to be determined for diseased appendages . There is a positive correlation between the serum PCT level greater than 0.5 µg / L and severe appendicular lesions. PCT mean increases with the severity of inflammatory lesions of the appendix (P =0.0051).

Sand[12] et al noted that the sensitivity of PCT for the diagnosis of acute appendicitis was 0.14, with a specificity of 1. The PPV of PCT (1 0.5 ng/ml) for appendicitis was 1 in contrast to 0.76 for CRP (1 0.5 mg/dl) and to 1 for WBC. The NPV for appendicitis were 0.06 for PCT, 0.09 for WBC and 0.11 for CRP. The values of CRP, WBC and PCT increased with the severity of the appendicitis.

Table 3: Present study compared to other studies

Study / parameter	*Age*	*Sample size*	*PCT cut off value*	*Sensitivity*	*Specificity*
PRESENT STUDY	***25***	***110***	***0.5***	***90***	***97.14***
Chandel	*Pediatric*	*40*	*0.7*	*100*	*100*
Gavela	*1.2-17.1*		*0.18*	*97*	*80*
Kafetzis	*Pediatric*	*212*	*0.5*	*73*	*95*
Kouame	*Pediatric*	*101*	*0.5*	*58*	*100*
Sand	*Adult*	*103*	*0.5*	*38*	*94*
Wu	*Adult*	*214*	*0.5*	*29*	*95*

VI. Conclusion

The PCT values can be used as predictor of complicated appendicitis & infectious complications following surgery for acute appendicitis and it can help to carry out timely surgical intervention which highly is recommended in patients with values more than 0.5ng/ml & also in this high litigation era , it can guide you to explain the incidence of possible surgical site complication in complicated appendicitis to the patients & its attendants.

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