TO DETERMINE THE ROLE OF CA125 IN THE DIAGNOSIS OF ACUTE APPENDICITIS
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Abstract
Background: the present study was under taken to determine the role of CA-125 in the diagnosis of acute appendicitis (AA), to prevent its complications and also in preventing negative appendicectomies in tertiary care hospital.

Methods: The study was conducted at a tertiary care and research center between 01/03/2018 to 30/06/2019. Patients admitted to the surgery department with diagnosis of AA were considered for the study. After informed consent, a, standardized history was obtained as a case Performa. Serum samples from all the cases with clinical diagnosis of AA were obtained and stored. Only the cases with histopathologically approved AA were included in the study. Cases operated for clinical diagnosis of AA, but not histopathologically proven AA was not included in the study. CA125 levels in cases with definitive diagnosis of AA were measured.

Results: In present study, ROC curve analysis revealed the sensitivity of 87.27 % and specificity of 90.91 % when the CA 125 cut-off value of > 16.8 was taken to diagnose acute appendicitis. AUC was 0.911 with a standard error of 0.0292.

Conclusion: In this study we have observed that CA125 showed a positive correlation with acute appendicitis, that was statistically not significant (P>0.05). We didn’t evaluate the correlation with the disease severity. We consider that CA125 can be used as a marker in acute appendicitis cases although further research is still needed.

Keywords: CA125, Acute Appendicitis, Surgery.

Introduction
Acute appendicitis (AA) is the most common surgical emergency in the world.¹ Despite diagnostic and therapeutic advances in medicine, appendicitis remains a clinical emergency if left untreated, having the potential for severe complications, including perforation or sepsis and may even cause death. The accurate and timely diagnosis of acute appendicitis plays an essential role in preventing such life-threatening complications.⁴

Despite more than 100 years of experience, accurate diagnosis still evades the surgeon and avoiding perforation and subsequent complications must be weighed against the removal of a normal appendix in patients with other causes of abdominal pain. Recently, a number of researches have been made for improving the medical treatment of AA.³⁵ In such an era of medical treatment, definitive diagnosis plays a very important role. Recent data support the evidence of successful medical treatment of uncomplicated AA cases.⁷ However, the main problem in these reports are that the exact number of negative appendicitis cases in medical treatment are not known.

There are several markers that are still being researched for definitive diagnosis of AA. Mainly leucocyte number and C - reactive protein are used as laboratory markers. However, they only indicate inflammation process and are not specific laboratory marker for AA.

Some studies have concluded that CA125 levels are significantly higher in patients with perforated or gangrenous appendicitis than patients with uncomplicated appendicitis.⁸ Some studies show that CA125 secretion begins six hours after the onset of inflammation, and in acute appendicitis where both visceral and parietal peritoneum are affected, CA125 should we elevated.⁹ CA125 is a glycoprotein secreted from mesothelium cells.¹⁰ It is mainly used in the diagnosis and the post operative follow-up of gynecological tumors,¹¹ liver cirrhosis and in pleural or peritoneal effusion and in conditions of peritoneal inflammations.

Hence, the present study was under taken to determine the role of CA-125 in the diagnosis of acute appendicitis (AA), to prevent its complications and also in preventing negative appendicectomies in tertiary care hospital.

Material and Methods
For this case control study ethical approval was obtained from ethical committee of SMS Medical College, Jaipur. The study was conducted at a tertiary care and research center between 01/03/2018 to 30/06/2019.
Inclusion criteria:
Histopathologically proven acute appendicitis patients.

Controls: Healthy volunteer as a control in my study who give written and informed consent.

Exclusion Criteria:
- Chronic Appendicitis
- Patients of CA ovary
- Patient of liver cirrhosis
- Immunocompromised patients

Preoperative Workup:

Patients admitted to the surgery department with diagnosis of AA were considered for the study. After informed consent, a standardized history was obtained as a case Performa. Serum samples from all the cases with clinical diagnosis of AA were obtained and stored. Only the cases with histopathologically approved AA were included in the study. Cases operated for clinical diagnosis of AA, but not histopathologically proven AA were not included in the study. CA125 levels in cases with definitive diagnosis of AA were measured.

For the control group, serum sample from healthy volunteers were obtained and CA125 levels were measured.

Follow Up

Histopathology report was obtained and compared with CA125 levels.

Data analysis

The data was tabulated, analyzed and the observations and results of the study discussed for arriving at conclusions regarding the sensitivity, specificity and positive predictive value.

**Results**

**Table 1:** Distribution of subjects according to Socio-demographic variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>Appendicitis Group (N=55)</th>
<th>Control Group (N=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean ± SD)</td>
<td>30.20 ± 17.74</td>
<td>40.76 ± 14.48</td>
</tr>
<tr>
<td>Male : Female</td>
<td>35 : 20</td>
<td>36 : 19</td>
</tr>
</tbody>
</table>

This observation correlates with the study of Addis In the present study out of 55 cases, 35 were male and 20 female and in control group out of 55, 36 were male and 19 were female. DG et al in which the incidence of appendicitis was found to peak in the 2nd to 4th decade of life.

**Table 2:** Distribution of mean CA125 levels in study subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Appendicitis Group (N=55)</th>
<th>Control Group (N=55)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA125 (Mean ± SD)</td>
<td>32.92 ± 15.13</td>
<td>9.41 ± 8.10</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Unpaired ‘t’ test

**Table 3:** ROC curve for CA125 value for diagnosis of acute appendicitis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area under the ROC curve (AUC)</td>
<td>0.911</td>
</tr>
<tr>
<td>Standard Error</td>
<td>0.0292</td>
</tr>
<tr>
<td>95% Confidence interval</td>
<td>0.842 to 0.957</td>
</tr>
<tr>
<td>z statistic</td>
<td>14.090</td>
</tr>
<tr>
<td>Significance level P (Area=0.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Youden index J</td>
<td>0.7618</td>
</tr>
<tr>
<td>Associated Criteria</td>
<td>&gt; 16.8</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>87.27</td>
</tr>
<tr>
<td>Specificity</td>
<td>90.91</td>
</tr>
</tbody>
</table>

In present study, ROC curve analysis revealed the sensitivity of 87.27 % and specificity of 90.91 % when the CA 125 cut-off value of > 16.8 was taken to diagnose acute appendicitis. AUC was 0.911 with a standard error of 0.0292.

**Table 4:** Correlation between appendicitis and control group CA 125 levels

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pearson’s Correlation coefficient (r)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA 125</td>
<td>0.047</td>
<td>0.733</td>
</tr>
</tbody>
</table>

It was observed in present study that CA 125 showed a positive correlation with acute appendicitis, that was statistically not significant (P>0.05). The Pearson’s correlation coefficient ‘r’ found to be 0.047 between two parameters.

The Pearson’s correlation equation was:

Y = 0.0252x + 8.57837

**Discussion**

Although the incidence of acute appendicitis has decreased slightly over the past few decades, it remains a common cause of acute abdominal pain and urgent surgical intervention. If untreated, acute appendicitis will progress from inflammation to perforation with abscess formation or diffuse peritonitis. However, misdiagnosis of acute appendicitis can result in unnecessary laparotomies. Generally, the morbidity and mortality of missing a case of acute appendicitis that subsequently develops peritonitis or abscess formation outweigh the complications associated with a negative appendectomy. Many inflammatory markers have been used to aid the diagnosis.
of acute surgical conditions, including appendicitis. Leukocyte count and C reactive protein concentration are the most commonly performed laboratory tests, with procalcitonin and D-dimers more recently proposed as novel biomarkers for acute abdominal disorders.\(^{12,13}\)

CA-125 is a 225 kDa glycoprotein produced by cells in the coelomic epithelium, the epithelium of the female genital tract, the colonic mucosa, stomach mucosa, and mesothelial cells in serous membranes.\(^{14}\) It is a cell-surface antigen recognized by the OC-125 antibody produced by OVCA433 cells, a carcinogenic ovarian epithelial cell line.\(^{15}\) This tumor marker is normally used to follow the clinical course of patients with ovarian cancer. In 80% of cases, its concentration increases, which is associated with disease progression or relapse.\(^{16}\) However, marked increases in plasma CA-125 concentrations also occur during pregnancy and following peritoneal irritation associated with infection or surgery, particularly pelvic inflammatory disease, benign ovarian cysts, ectopic pregnancy, and fibroids. Its levels also increase by up to two times during menstruation.\(^{17}\) Several studies\(^ {18,19}\) have also suggested that the peritoneum is an important source of CA-125, and that peritoneal inflammation contributes to increases in its serum concentrations in pathological conditions. Inflammatory disorders, including pelvic inflammatory disease, endometriosis (especially with adhesions), malignant pathologies with ascites, and peritonitis are associated with high circulating CA-125 concentrations. From this context, we evaluated the diagnostic potential of CA-125 in acute appendicitis. Here, we found that patients with acute appendicitis had significantly greater CA-125 concentrations compared with healthy subjects. In the disease process, acute appendicitis starts as a localized inflammatory process and may progress from localized peritonitis to generalized peritoneal inflammation. Accordingly, an increase in CA-125 concentration may be due to peritoneal inflammation, which can involve two mechanisms. First, CA-125 released from damaged peritoneal mesothelial cells is absorbed and transferred to the circulation. Second, Zeillemaker et al. reported that the secretion of CA-125 from a monolayer of mesothelial cells into culture medium can be enhanced by the inflammatory cytokines interleukin-1β, tumor necrosis factor, and lipopolysaccharide.\(^ {20}\) Therefore, during the disease process in vivo, increased cytokine levels may augment the secretion of CA-125 from the peritoneal surface.

**Conclusion**

In this study we have observed that CA125 showed a positive correlation with acute appendicitis, that was statistically not significant (P>0.05). We didn’t evaluate the correlation with the disease severity. We consider that CA125 can be used as a marker in acute appendicitis cases although further research is still needed.

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