

Role Of Total Leukocyte Count, Neutrophil Percentage, C-Reactive Protein And Ultrasonography In The Diagnosis Of Acute Appendicitis.

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Citation

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Abstract

Total leucocyte count (TLC), neutrophil percentage (NP), C-reactive protein (CRP) and ultrasonographic (USG) examination of the abdomen were studied prospectively in 197 patients who underwent appendectomy for suspected appendicitis. On histopathological study of the resected appendices, only 176 patients had acutely inflamed, perforated or gangrenous appendices. The sensitivity, specificity and predictive value of single tests and test combinations were calculated using standard reference intervals. CRP demonstrated the best sensitivity (89%) followed by ultrasonography (78%), though the best specificity (90.47%) was observed in the latter test. The sensitivity decreased when raised TLC, NP, CRP and suggestive USG were used together to predict appendicitis but the specificity increased markedly (95%) indicating the fact that acute appendicitis is unlikely when all these tests are simultaneously negative. Early USG, preferably combined with CRP, and leucocyte counts is a very useful diagnostic aid in acute appendicitis and clinicians should suspect that appendicitis is less likely if all four investigations are simultaneously negative.

INTRODUCTION

Acute appendicitis is one of the most frequent causes of acute abdomen in nearly all age groups (1) and hence appendectomy is one of the most common surgeries being performed world wide. The diagnosis remains one of the most difficult clinical problems in abdominal emergencies with reported diagnostic accuracy varying from 25-90 % (2). A retrospective review of 1,243 appendicitis patients has shown that normal appendices were removed in 25.7 % (3) while another review revealed 13.5 % normal appendices at laparotomy (4). It is believed that the optimal accuracy rate is around 80 %, since a less than 20 % negative appendectomy rate would involve a high perforation rate (<20%) with resultant complications (2). The negative exploration itself carries a complication rate not much lower than that after removal of a pathological appendix (5). This warrants supplementary investigations that can improve diagnostic accuracy and further reduce the number of negative appendectomies without thereby increasing the perforation rate.

In acute appendicitis, TLC and NP are the most frequently

used laboratory tests (6). Most of the studies conclude that 60-90 % of all patients with acute appendicitis have total and differential leucocyte counts suggestive of the diagnosis (5). CRP is an acute phase reactant, synthesized by liver which exhibits an exponential rise in serum concentration within eight hours in bacterial infection (7, 8). It also appears in the sera of individuals in response to a variety of inflammatory conditions and tissue necrosis.

USG, if performed by proper hands, has a specificity of 85-95% (9, 10, 11) but due to its variable sensitivity, it is not used as a routine test (12). However some authors believe that immediate use of USG examination of the abdomen helps in improving the diagnostic acumen (13).

AIM OF THE STUDY: To evaluate prospectively the clinical applicability of TLC, NP, CRP, and USG in acute appendicitis. The study was designed to assess the significance of the tests (separately and jointly) in patients operated for acute appendicitis.

MATERIALS AND METHODS

During a period of 12 months, 197 consecutive patients between the ages of 12 and 60 years operated upon for

suspected acute appendicitis were included in this prospective study. This study was conducted in the Department of General Surgery of a tertiary health care institute catering Jammu and Kashmir State of India. Children below 12 years were not included as they are managed by the pediatric surgery unit of our hospital which did not participate in this study. Due to the prevailing set-up, appendicectomies are usually performed as an emergency surgery, predominantly by junior surgeons (registrars). We do not have the facility to do laparoscopy in the emergency theatre room. A formal consent from the local ethical committee was taken by the authors for this project as this was the thesis work assigned to the prime author.

Venous blood was routinely taken on admission and was sent to the emergency laboratory where TLC was determined by the vesical method (14) using an improved Neubauer chamber. NP was determined immediately by counting 100 white cells on a peripheral smear. The upper limit of the TLC was taken as $10 \times 10^9/L$ and that of the NP as 75% (15).

CRP was quantified using a commercially available CRP kit (CRP latex test, Randox Laboratories Ltd., UK) and the manufactures instructions and reference interval. The test was read as positive with the screen CRP levels $>6\text{mg/l}$.

USG was performed on all these patients in the Department of Radio-Diagnosis by 5MHz-linear probe with graded compression. Visualization of the appendix alone was taken as a sign of appendicitis, located para-caecal fluid or para-appendicular fat $>10\text{mm}$ and appendicolith were other USG findings suggestive of appendicitis. Other abdominal and pelvic pathologies were also looked for.

The diagnosis was finally confirmed when transmural acute inflammatory changes were seen on histopathological examination. The distinctions between gangrenous and perforated appendices were made on the operative appearance by the surgeon.

OBSERVATIONS

Table 1 gives the diagnosis obtained after laparotomy conducted on 197 patients of suspected acute appendicitis. Appendicitis was confirmed in 176 patients by histopathological examination. Nine patients had perforated appendices while 10 had gangrenous ones (Table 11). In 10 patients, the cause of pain could not be fathomed while it was evident in other 11 patients. Hence, the total number of negative surgeries was 21 (10.65%). Although the

male/female distribution was almost equal, two-thirds of the normal appendices were found in women. No significant sex-related differences were found in the incidence of perforated or gangrenous appendicitis. Leucocytosis (Table 11) was observed in 141 patients while appendicitis was confirmed in 134 patients only. Forty-two patients with appendicitis had normal leucocyte counts. Overall, 134 had increased TLC (sensitivity 76.13%). Elevated NP (Table IV) was observed in 103 patients of acute appendicitis while the rest (73 patients) had normal NP. With the combination of the above 2 tests, joined by an 'or' rule (if any of the individually linked tests of the combination was above the reference range, the combination was considered indicative of acute appendicitis), the sensitivity rose to 86.93% ($\chi^2=24.3124$; >0.05) but the specificity decreased to 57% (Table V). CRP alone was seen elevated in 158 of 176 patients (89.72%) with acute appendicitis and 9 other patients who had a normal appendix (Table VI). Using the 'or' rule in the combination of raised TLC, NP and CRP, the sensitivity increased to 92.04% with a specificity of 61.9% (Table VII). Ultrasonography done on these patients revealed that out of 21 negative explorations, 19 patients had a normal ultrasonography reporting (Table VIII) and the investigations were suggestive in 137 of the 176 appendicitis patients (sensitivity of 77.84%). USG was the most specific of all investigations under evaluation (90.99%). With the use of the "or" rule (Table IX), USG in combination with raised TLC, NP and CRP improved the sensitivity to 97.15% but had low specificity (47.61%). On the other hand, if all four tests were combined (+) and were simultaneously negative, they were highly specific in ruling out appendicitis (specificity 95.23%) (Table X). Individually, all tests except neutrophil percentage had statistically significant correlation with acute appendicitis which is a well proved fact. But as far as the aim of present study is concerned, all four investigations together would help in reducing negative laparatomies, as 20 of the 21 patients in whom appendicitis was not present had all four investigations simultaneously negative. The overall sensitivities and specificities are summarized in table XI.

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Figure 1

TABLE I: Diagnosis at Laparotomy

| | | |
|-------------------------|------------|-----|
| Acute Appendicitis | 158 | 176 |
| Perforated Appendix | 7 | |
| Gangrenous Appendix | 11 | |
| Torted Ovarian Cyst | 3 | 21 |
| Salpingo-oophoritis | 3 | |
| Pelvic Peritonitis | 2 | |
| Ruptured Ovarian Cyst | 1 | |
| Tubal Pregnancy | 1 | |
| Meckel's Diverticulitis | 1 | |
| Negative Exploration | 10 | |
| TOTAL | 197 | |

Figure 2

TABLE II: Sex Distribution

| Sex | Total Number | Inflamed | Gangrenous | Perforated | None |
|-----|--------------|-------------|------------|------------|-------------|
| M | 95 | 78 (82.10%) | 4 (4.21%) | 6 (6.31%) | 7 (7.36%) |
| F | 102 | 80 (78.43%) | 3 (2.94%) | 5 (4.90%) | 14 (13.72%) |
| | 197 | 158 | 07 | 11 | 21 |

$X^2 = 2.2050 \Rightarrow p > 0.05$ (NS)

Figure 3

TABLE III: TLC vs Appendicitis

| TLC | Appendicitis | | Total |
|--------------|--------------|-----------|------------|
| | + | - | |
| ↑ed | 134 | 7 | 141 |
| N | 42 | 14 | 56 |
| Total | 176 | 21 | 197 |

$X^2 = 16.8943 \Rightarrow p < 0.05$

(+ is in pts confirmed to have appendicitis/ - is in pts not having appendicitis or having other pathologies/ n is normal counts/led is raised counts)

Figure 4

TABLE IV: NP vs Appendicitis

| NP | Appendicitis | | Total |
|--------------|--------------|-----------|------------|
| | + | - | |
| ↑ed | 103 | 8 | 111 |
| n | 73 | 13 | 86 |
| Total | 176 | 21 | 197 |

$X^2 = 31.1828 \Rightarrow p > 0.05$

Figure 5

TABLE V: TLC or NP vs Appendicitis

| TLC or NP | Appendicitis | | Total |
|-----------|--------------|-----------|------------|
| | + | - | |
| ↑ed | 153 | 8 | 161 |
| n | 23 | 13 | 36 |
| | 176 | 21 | 197 |

$X^2 = 29.9613 \Rightarrow p < 0.05$

Figure 6

TABLE VI: CRP vs Appendicitis

| CRP | Appendicitis | | Total |
|--------------|--------------|-----------|------------|
| | + | - | |
| ↑ed | 158 | 9 | 167 |
| n | 18 | 12 | 30 |
| Total | 176 | 21 | 197 |

$X^2 = 31.176 \Rightarrow p < 0.05$

Figure 7

TABLE VII: TLC or NP or CRP vs Appendicitis

| Tests | HPE | | Total |
|--------------|------------|-----------|------------|
| | + | - | |
| ↑ed | 162 | 9 | 171 |
| n | 14 | 12 | 26 |
| Total | 176 | 21 | 197 |

$X^2 = 39.6235 \Rightarrow p < 0.05$

Figure 8

TABLE VIII: USG vs Appendicitis

| USG | HPE | | Total |
|------------------------|------------|-----------|------------|
| | + | - | |
| Diagnostic of app. | 137 | 2 | 139 |
| Not diagnostic of app. | 39 | 19 | 58 |
| Total | 176 | 21 | 197 |

$X^2 = 42.1516 \Rightarrow p < 0.05$

Figure 9

TABLE IX: TLC/NP/CRP/USG (or) vs Appendicitis

| Tests | HPE | | Total |
|--------------|------------|-----------|------------|
| | + | - | |
| ↑ed | 171 | 11 | 182 |
| n | 5 | 10 | 15 |
| Total | 176 | 21 | 197 |

$X^2 = 53.4771 \Rightarrow p < 0.05$

Figure 10

TABLE-X: All Positive (Combining) vs Appendicitis

| ↑Test | HPE | | Total |
|-------|-----|----|-------|
| | + | - | |
| ↑ed | 92 | 1 | 93 |
| n | 84 | 20 | 104 |
| Total | 176 | 21 | 197 |

$X^2 = 16.9929 \Rightarrow p < 0.05$

Figure 11

Table XI: Comparison of Results of Various Tests or Test Combinations

| Investigation | Sensitivity % | Specificity % |
|---------------------------|---------------|---------------|
| TLC | 73.13 | 66.66 |
| NP | 58.52 | 61.90 |
| TLC or NP | 86.93 | 57.14 |
| CRP | 89.72 | 57.00 |
| TLC/NP/CRP (or) | 92.04 | 61.90 |
| USG | 77.84 | 90.47 |
| TLC/NP/CRP/USG (or) | 97.15 | 47.61 |
| TLC+NP+CRP+USG(combining) | 52.27 | 95.23 |

DISCUSSION

The cause of right iliac fossa pain continues to elude surgeons for more than a century. The cause may be acute appendicitis which requires surgery or something else that may not require intervention. To resolve the dilemma, a study was conducted in the SKIMS to determine the role of investigations (TLC, NP, CRP and USG) in the patients operated for suspected appendicitis. A study sample was formed by 197 subjects operated for appendicitis on the basis of suggestive clinical and/or paraclinical parameters.

A similar study was conducted by Amrita et al. and Singh et al. (16,17), where they concluded that these investigations should be interpreted in light of clinical findings.

The majority of patients with acute appendicitis have an elevated total leukocyte count of more than ten thousand (18). It was observed in this study that the initial leucocyte count was elevated in 141 out of a total of 197 patients taken for laparotomy. Histological confirmation could be made in 134 patients only, giving a sensitivity of 76.13% and a specificity of 66.70%. Higher mean TLC values were observed in gangrenous and perforated appendices which are summed up in a different article in order not to make the present study to large. Leu et al. found an elevated leucocyte count in 81.4% of patients with a specificity of 77.3% (19). Most of the studies reveal that >60% of patients with acute appendicitis have a TLC of over $10 \times 10^9/l$ (20, 21). Since

the white cell count is raised in 25-70% of patients with other causes of acute right iliac fossa pain (5), the investigation is rendered almost useless by its low specificity and has little diagnostic value (2,5).

It was observed in this study that raised NP was less sensitive (58.52%) and specific (61.90%) with higher mean values in gangrenous/perforated appendicitis. The sensitivity of raised NP ranges from 60 to 84% in various studies (22,23,24). The sensitivity improved to 87% while the specificity continued to be low when raised TLC and raised NP was combined by the 'or' rule. Similarly, comparable results of 90.5% (sensitivity) and 58.8% (specificity) were observed by Lau et al. (19).

Many previous studies have observed that an increased CRP reveals acute appendicitis and claim it to be a highly sensitive investigation. Dueholm (25) observed that CRP had a sensitivity of 75% and specificity of 56%, while Thompson et al. reported a sensitivity of 69% and specificity of 75% in acute appendicitis (26). The present study depicted a high sensitivity of 89.7% with a specificity of 57% only. Higher values were observed by Daves (27) (sensitivity of 94% and specificity of 75%) as well as Amrita Verma et al. (14). This could be due to the fact that 11 out of 21 negative explorations were inflammatory conditions and 8 of them had elevated CRP levels proving the fact that the levels are seen to be increased in diseases other than appendicitis (28). Adding CRP to the TLC and NP makes it a highly sensitive combination.

Ultrasonography, besides being highly specific in diagnosis acute appendicitis, accurately excludes diseases that do not require surgery. Most of the American and European studies give high sensitivities of 80-90% and specificities of 94-100% (29). Less accurate results in another study (30) and low values obtained in the present study could be due to the fact that the probe used was 5MHz in contrast to 7.5MHz used by them. Poorer results are also observed for retro-caecal appendices (31) which, in the present study, were seen in 39 patients and only 12 of them were picked up by USG. Also, it is technically difficult to detect an inflamed appendix in obese or distended patients. We would also like to remark that the results are operator-expertise dependent.

The present study revealed that 18 of the total of 19 gangrenous/perforated appendices were picked up by USG (>94%), though the sonologist did not make the diagnosis of perforated or gangrenous appendicitis. Takeda et al.

observed a sensitivity of 100% in such cases. Combining the previous three investigations to USG by the 'or' rule raises the sensitivity to >90%, but the specificity continued to be low (47%). In contrast, sensitivity decreased and specificity increased markedly when all the 4 suggestive investigations were used together.

CONCLUSION

It must be emphasized that the total and the differential cell counts should be interpreted in the light of physical findings as normal counts do not exclude appendicitis and raised counts and raised NP can occur even in normal patients. The CRP is a better indicator of appendicitis than TLC and NP. In view of its high sensitivity and specificity, USG promises to be the investigation of choice. This test is non-invasive and can be of particular help in pregnancy (5) but its main disadvantage lies in the fact that it requires special equipment and special expertise. Hence, the decision against laparotomy, however, must always be based on the clinical findings which are the mainstay of the diagnosis. In the present era of laparoscopic surgery, ruling out appendicitis may not be a major problem (32), but we understand that if the patient undergoes anesthesia and laparoscopy with the diagnosis not being appendicitis, it does not amount to anything less than laparotomy. Another aspect is that others may argue that this is an era of CT imaging and CT would give better diagnostic accuracy (33); but in a developing country like ours we understand that doing CT scan is not very cost effective. We conclude that these simple investigations, if simultaneously not suggestive of the diagnosis, rule out appendicitis and in such a situation surgeons should rather choose a conservative approach than a negative laparotomy.

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Role Of Total Leukocyte Count, Neutrophil Percentage, C-Reactive Protein And Ultrasonography In The Diagnosis Of Acute Appendicitis.

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