

## PROSPECTIVE STUDY TO EVALUATE APPENDICITIS INFLAMMATORY RESPONSE SCORE AND CT-SCAN TO DIAGNOSE ACUTE APPENDICITIS

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### Abstract

**Background:** Appropriately diagnosing Acute Appendicitis is important, in terms of preventing misdiagnosis leading to delay in diagnosis and consequently developing complications of acute appendicitis and increase in morbidity. Secondly to avoid misdiagnosis related to negative explorations for appendicitis. We compared AIR (Appendicitis Inflammatory Response) score and CT scan of abdomen to reach to an appropriate diagnosis of acute appendicitis and to get indications for doing CT scan of abdomen. The aim is to evaluate the AIR score. To find indications of CT scan in Acute Appendicitis. **Materials and Methods:** Prospective, Observational study conducted in a tertiary care, teaching hospital for a period of 18 months, in 100 cases of suspected acute appendicitis. The hospital ethics committee clearance was obtained prior to undertaking the study. **Result:** In AIR score, maximum specificity and sensitivity was found at a cut off of 7; sensitivity of 86.3% and specificity of 93.9. By comparing the positive likelihood ratios of AIR score and CT scan we found that in patients with AIR scores of 8 and above, CT scan evaluation is not warranted and directly surgery can be planned. CT scan is to be done in patients with AIR score of 7 and below. **Conclusion:** Our study, has shown that AIR score has provided us information regarding patients who need urgent surgery, patients who can be conserved and patients who need further follow-up and evaluation by AIR score or Imaging studies.

## INTRODUCTION

The diagnosis of acute appendicitis depends on the experience of the surgeon, appropriate utilization of appendicitis scores and CT scan of abdomen. The negative laparotomy rate ranges from 17% to 36% and is associated with significant morbidity.<sup>[1]</sup> Negative explorations for appendicitis causes stress of anaesthesia and surgery as well as socio economic stress, loss of working hours for the patient. Secondly more challenging is to appropriately diagnose an Acute Appendicitis, so that we should avoid any delay in emergency appendectomy, thereby preventing further complications and morbidity. We chose to apply AIR score for our patients [Table 1]. Many of the surgeons are resorting to CT scan of abdomen for diagnosing acute appendicitis. This cause economic burden as well as unnecessary radiation to the

patient. So, to prevent negative appendectomies, to prevent delay in surgery, minimising the rate of CT scan, at the same time to find appropriate indication for CT scan of abdomen, we conducted this study.

## MATERIALS AND METHODS

This was an observational and prospective study conducted in a tertiary care teaching hospital for a period of 18 months, in 100 cases of suspected acute appendicitis. The hospital ethics committee clearance was obtained prior to undertaking the study.

Sampling method was convenience consecutive consenting. Patients evaluated in the emergency department with a suspicion of acute appendicitis were included in the study and assessed by appendicitis inflammatory response score [Table 1]. For some patients CT scan of abdomen and pelvis,

was done according to the decision of a senior surgeon. A senior surgeon decided if the patient required emergency open appendectomy or conservative management on the basis of his/her clinical evaluation, WBC count, USG and CT findings. Presence and type of appendicitis was gauged by the intra operative findings and histopathology report. Patients managed conservatively were followed up after one month to check if they developed the symptoms again and required admission and/or surgery for acute appendicitis.

#### **Inclusion Criteria**

- Patients between the age group of 12 to 60 years.
- Patients clinically suspected to have acute appendicitis.
- All male and female patients.

#### **Exclusion Criteria**

- Patients clinically not suspected to have appendicitis.
- Patients having previous abdominal surgery done.
- Patients who are a known case of Koch's abdomen.
- Patients not giving consent.
- Patients with urinary pregnancy test positive.
- Interval appendectomies

Appendicitis was considered present when patients who had undergone surgery had final histology showing acute appendicitis. A case was labelled negative appendectomy when patient's histopathology report was negative (histopathology report of chronic appendicitis was taken as negative). Patients who were managed conservatively and did not develop abdominal pain or require appendectomy within one month of follow up were considered to not have appendicitis. A patient was labelled as missed diagnosis if within one month of discharge they developed appendicitis and required an appendectomy. CT scans were read by radiologist on duty and were labelled as positive or negative.

Sensitivity, specificity, positive predictive value, negative predictive value and likelihood ratios were calculated for each off the cut off scores of AIR score ranging from 3 to 12. The same performance measures were evaluated for CT scan using the same gold standard.

The range of AIR for which patient were least likely to benefit from CT evaluation were estimated by comparing the positive likelihood ratios of the AIR ranges with that of CT scan. Likelihood ratios were selected as the deciding parameter because they are independent of disease prevalence and depend on the ability of the test to distinguish between disease and non-disease.

Patient baseline characteristics were summarized with descriptive statistics. Continuous variables were summarized with descriptive statistics (n,

mean, standard deviation, median, interquartile range, minimum, maximum). Categorical variables were summarized with counts and percentage.

Diagnostic accuracy measure such as, sensitivity, specificity, positive and negative predictive values were used to analyse primary objective of the study with gold standard Histopathological examination.

We constructed receiver operator characteristic (ROC) curve for appendix inflammatory score to determine its ability for diagnosing acute appendicitis. The optimal cut - off values were obtained with the greatest sum of sensitivity and specificity using the Youden Index. Descriptive statistics was used to evaluate the rate of negative appendectomies and any missed diagnosis of acute appendicitis.

A p-value  $\leq 0.05$  in a two-tailed test was considered statistically significant. Statistical analyses were performed using SPSS (the statistical package for social sciences) IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp and BDT comparator program.

## **RESULTS**

The mean age of patients was 30.28 years. The maximum number of patients presented in the age group of 21- 30 (36%). There were 55 male and 45 female patients. Of the 45 females, 23 were diagnosed as having appendicitis and of the 55 males 28 had acute appendicitis.

Of the 100 patients taken in the study, 90% complained of vomiting and 98% had pain in the right iliac fossa. Rebound tenderness was observed in 74% of them and raised temperature ( $> 38.50^{\circ}\text{C}$ ) seen in 42%. Leucocytosis of more than 10000/mm<sup>3</sup>, was seen in 81% of the patients. Polymorphonuclear leucocytosis of more than 70% was seen in 78% of the cohort. CRP was above 10 g/L in 90% of the study group.

The AIR score was analyzed for all the 100 patients. In this study, the minimum score was of 3 and maximum of 12. The score was divided into three types – low probability (0 - 4), intermediate probability (5 - 8) and high probability (9 – 12). Of the 100, 41 patients were in the low probability score ranges, 39 in intermediate and 20 in high probability scores. Amongst the conserved the diagnosis was arrived upon on the basis of clinical evaluation, USG findings or CT scan findings.

#### **Low Probability**

There were 41 in this category of which 4 were in the operated category and 37 conserved. Among these, 46.3% were suffering from renal colic, 29.2% were diagnosed with colitis, PCOS and abdominal Koch's. Even in these low scores four patients were operated on advise of senior surgeon depending upon clinical examination findings. However, on histopathology findings one of them had chronic

appendicitis, one had phlegmonous appendicitis and two had catarrhal appendicitis.

#### Intermediate Probability

There were 39 in this category of which 8 patients were conserved and 31 were operated. Of the 31 operated, 17 had catarrhal appendicitis, 6 had phlegmonous, 2 were perforated, one was gangrenous appendix and five chronic appendicitis. In the conserved group, one case of appendicular lump and 3 cases of abdominal Koch's was present.

#### High Probability

All patients in this category were operated. 45% of patients, had a perforated appendix and none had chronic appendicitis. Majority of the patients with these higher scores had an advanced form of appendicitis.

#### CT scan Findings

In this study CT scan was done for 47 patients. Of these, 6 were in the high probability category, 20 in intermediate and 21 in low probability. Decision to do CT scan was taken by senior surgeon and was mostly done to rule out other causes of right sided, abdominal pain. Of the 47 CT scans done, 21 had appendicitis, 2 had appendicular lump, 8 were diagnosed as abdominal tuberculosis and 9 had a normal scan.

Of the 47 CT scans done, 6 were for people with AIR range in high probability and all were Positive for acute appendicitis. In the low probability category 17 of the 21 scans done were negative for acute appendicitis and only four detected appendicitis. In intermediate category, 13 of 20 scans were positive and 7 were negative.

#### Histopathology Findings

Out of total 55 patients who were operated, histopathology revealed, 38.2% were catarrhal appendicitis, 25.4% had phlegmonous appendicitis, 20% perforated, 5.4% Gangrenous and 10.9% were chronic appendicitis.

#### Air Score Analysis

1. Sensitivity and specificity at AIR score Cut off value of 4 all patients with AIR scores above 4 were taken as positive and below as negative. Using the above formulae, all the parameters for an AIR score cut off of 4 was calculated [Table 2].
2. Sensitivity and specificity at AIR score Cut off value of 8 all patients with AIR scores above 8 were taken as positive and below as negative. Using the above formulae, all the parameters for an AIR score cut off of 8 was calculated [Table 3].
3. Sensitivity and specificity were calculated for the AIR scores from 3-12[Table 4].
4. Receiver operator characteristic curve

The receiver operating characteristic curve of diagnosing acute appendicitis for appendix inflammatory score was plotted. The area under the ROC curve was 0.96 (Predictive accuracy), with 95% confidence interval (0.93-0.99) which shows a good fit (P value < 0.001). This shows that the test has a good discrimination between patients with disease and no disease [Figure 1].

#### CT Scan Analysis

CT scan was done in 47 patients. Among which, 23 CT scan came positive for appendicitis, of which 22, were positive and one was negative for appendicitis as per histopathology report. Out of 24 negative CT scan, 23 were reported negative for appendicitis and one was positive for appendicitis as per histology. Using the above formulae, all the parameters for CT scan was calculated [Table 5].

#### Positive Likelihood Ratios

Positive likelihood ratio was calculated for all the AIR scores and CT scan. Positive likelihood ratio of CT scan is superior to the AIR score of 7 and below. AIR score of 8 and above have a positive likelihood ratio higher than CT scan [Table 6].

**Table 1: AIR Scoring sheet with proposed clinical algorithm**

<b>Vomiting</b>		<b>1</b>
Pain in right inferior fossa		1
Rebound tenderness or muscular defense	Light Medium Strong	1 2 3
Body temperature $\geq 38.5$		1
Polymorphonuclear leucocytes	70-84% $\geq 85\%$	1 2
WBC counts	10.0-14.9 $\times 10^9 / L$ $\geq 15.0 \times 10^9 / L$	1 2
CRP concentration	10 -49 g/L $\geq 50 g/L$	1 2
Sum 0-12		

Sum 0–4 = Low probability. Outpatient follow-up if unaltered general condition

Sum 5–8 = Indeterminate group. In-hospital active observation with rescoring/imaging or diagnostic laparoscopy according to local traditions

Sum 9–12 = High probability. Surgical exploration is proposed

**Table 2: Sensitivity And specificity of AIR score at cut off value of 4.**

Statistic	Value	95% CI
Sensitivity	100.00%	93.02% to 100.00%
Specificity	28.57%	16.58% to 43.26%
Positive Predictive Value (*)	59.30%	54.97% to 63.50%
Negative Predictive Value (*)	100.00%	

**Table 3: Sensitivity And specificity of AIR score at cut off value of 8.**

Statistic	Value	95% CI
Sensitivity	68.63%	54.11% to 80.89%
Specificity	100.00%	92.75% to 100.00%
Positive Predictive Value (*)	100.00%	
Negative Predictive Value (*)	75.38%	67.11% to 82.13%

**Table 4: Sensitivity And specificity of AIR score at cut off value of 3-12**

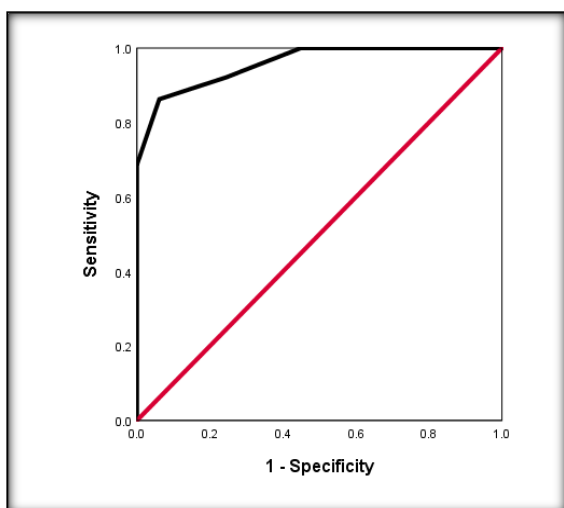
Appendix Inflammatory Score (n= 100)	Sensitivity (95% CI)	Specificity (95% CI)
≥3	100%	0%
≥4	100%	28.6%
≥5	100%	55.1%
≥6	92.2%	75.5%
≥7	86.3%	93.9%
≥8	68.6%	100%
≥9	41.2%	100%
>10	29.4%	100%
≥11	7.8%	100%
≥12	2%	100%

**Table 5: Sensitivity and specificity of CT scan of Abdomen for diagnosing Appendicitis.**

Statistic	Value	95% CI
Sensitivity	95.65%	78.05% to 99.89%
Specificity	95.83%	78.88% to 99.89%
Positive Likelihood Ratio	22.96	3.36 to 156.70
Positive Predictive Value (*)	95.65%	76.32% to 99.34%
Negative Predictive Value (*)	95.83%	77.15% to 99.37%

**Table 6: Positive likelihood ratio for all the AIR scores and CT scan**

	Positive likelihood ratio
CT scan (n = 47)	22.96(3.36 – 156.70)
AIR scores (n = 100)	
≥3	1.000 (0.983- 1.018)
≥4	1.397 (1.170- 1.669)
≥5	2.223 (1.630- 3.032)
≥6	3.763 (2.287- 6.193)
≥7	14.092 (4.682-42.412)
≥8	336.961 (0.688-165112.462)
≥9	202.176 (0.410-99654.038)
≥10	144.412 (0.291-71602.507)
≥11	38.510 (0.073-20203.505)
≥12	29.627 (0.015-6331.303)

**Figure 1: ROC Curve**

[Figure 1] The area under the ROC curve was 0.96 (Predictive accuracy), with 95% confidence interval (0.93-0.99) which shows a good fit (P value < 0.001).

## DISCUSSION

Acute appendicitis is the most common cause of acute abdomen. Approximately 7% of the population will be affected by this condition during full life [2]. Commonly, right lower quadrant of acute abdominal pain is clinically diagnosed as acute appendicitis. But there are other important differential diagnoses of Right Iliac Fossa pain, so the diagnosis of acute appendicitis still remains a challenge. So appropriate diagnosis either by laboratory and or radiological means is necessary.

The new generation of Surgeons and Radiologist, advise CT scan abdomen for diagnosis of any acute abdomen. However, imaging does not perform well in patients with low and high prevalence of the disease, and CT should be used selectively to minimize exposure of ionizing radiation.<sup>[3]</sup> CT can provide information of diameter of appendix, peri appendicular fluid, appendicular abscess, mass and perforation of appendix, as well as any other acute abdominal pathology. The disadvantages of CT scan are radiation exposure, contrast-agent toxicity, and the requirement of experienced radiologist for interpretation in emergency situations. An abdominal-pelvic CT scan would typically lead to an effective dose of 10 mSv, which is an equivalent of 4.5 years of natural background radiation<sup>[4]</sup>. This warrants the need for an efficient scoring system that can use basic, easily accessible parameters and accurately diagnose acute appendicitis. AIR score was developed in 2008, by Andersson M et al<sup>[5]</sup>. This score is simple and the majority of patients who are suspected to have appendicitis can be diagnosed correctly. Their study showed that radiological investigations will be needed to few patients with an indeterminate scoring result. R E B Andersson, in his study mentioned that clinical history of migration of pain, blood investigations like granulocyte count, proportion of polymorph nuclear blood cells, WBC counts, C-reactive protein concentration and clinical examination parameters of rebound tenderness, guarding and rigidity, when considered together provided better diagnostic yield.<sup>[6]</sup>

According to de Castro et al, AIR score is better than Alvarado score when analysing women, children, and the elderly.<sup>[7]</sup> They also found that, negative appendectomy rate could have potentially declined from 10% in their study cohort to 2% with the AIR scoring system.

The present study evaluates the efficacy of the AIR score in 100 patients from our hospital, who were suspected to have acute appendicitis and attempted to correlate it with the efficacy and need of CT scan. Our study shows that the AIR score has a good statistical discrimination for patients with acute appendicitis. In this study it was found that the score has very high sensitivity (100%) but very low specificity (28%) when the cut off is kept at 4. This means that this score at a cut off of 4 can predict the positive cases but cannot rule out negative ones efficiently. At a cut off of 8, the sensitivity was 68% but specificity 100%. Maximum specificity and sensitivity were found at a cut off of 7; sensitivity of 86.3% and specificity of 93.9%. Thus, in the present study, we found that at a cut off of 7 the score is good at both predicting positive cases and ruling out cases that do not have appendicitis. In the study by De castro et al, a cut off of 4 was found to have a good sensitivity and a fair specificity of 85%<sup>[7]</sup>. A study by Patil S et al, found only a 63.6% specificity at a cut off of 4.<sup>[8]</sup> However all the reviewed studies established that the specificity is 100% at a cut off

of 8 and sensitivity is high at a cut off of 4.

Andersson M, in his study proposed that, the AIR score has reported an ROC area of the 0.97 for advanced appendicitis and 0.93 for all appendicitis.<sup>[5]</sup> In our study, the area under the ROC curve was 0.96 (Predictive accuracy), with 95% confidence interval (0.93-0.99) which shows a good fit (P value < 0.001). Thus, it was seen in this study that AIR score has a good discrimination capacity, just as it was seen in the other studies. This shows that the test has a good discrimination between patients with disease and no disease. Meer, M Chisti et al, suggested that, the area under the ROC curve for the RIPASA and AIR scoring systems was significantly larger than it was with the Alvarado system. The RIPASA and AIR scores are fast and are definitely better in categorizing patients with suspected appendicitis and reduce the need for diagnostic imaging<sup>[9]</sup>.

Our CT scan results for diagnosing acute appendicitis showed high specificity and sensitivity of 96%, specificity 96%, PPV 0.96, NPV 0.96 and a positive likelihood ratio of 22.36. Rud B, et.al, concluded that, the specificity and sensitivity of CT is high for diagnosing acute appendicitis in an adult.<sup>[10]</sup> But it was found that the median dose of a routine abdomen and pelvis was 66% higher.<sup>[11]</sup> This increases the risk of cancer in the patients.

Thus, one of the motives of this study was to identify AIR ranges that would benefit with CT evaluation. This will prevent doing CT for all the patients suspected to have appendicitis and thus decrease the radiation related risk of cancer. Our data indicates that CT evaluation has value mainly in patients with AIR score of 7 and below; the positive likelihood ratio of CT was significantly superior to the positive likelihood ratio of the AIR within these score ranges. So according to this study, patients with AIR score of 8 and above are unlikely to benefit from CT scan because the positive likelihood ratios of the AIR scores within these score ranges were not significantly different from that of CT scan. A similar such study was conducted by Tan W J et al but with Alvarado Score and CT scan; here they concluded that males with AS of 7 and above and females with AS of 9 and above were unlikely to benefit from CT evaluation because the positive likelihood ratios of the AS within these score ranges were similar to those of CT scan.<sup>[12]</sup>

Two cases of appendicular lump were present in this study with an AIR score of 5 and 6. Both patients were rightfully subjected to a CT evaluation and were conserved. Thus, this concurs with our study finding that an AIR score of 7 and below will benefit with further radiological evaluation.

There were 25 patients with a score of 8 and above who were operated without a CT scan evaluation and none of them showed a histopathology report

with normal appendix. Hence, this supports the claim that at an AIR score of 8 and above CT evaluation is unnecessary.

Of the 100 patients in the study, 55 were taken up for emergency open appendectomy by the senior surgeon. Of these 55 appendectomies, 20 had AIR scores in the high probability group. Intra-operative findings and histology diagnosed it as an acute appendicitis. Thirty-One appendectomies were in the intermediate probability group of which, histopathology revealed, 26 patients had acute appendicitis and 5 had chronic appendicitis. Four appendectomy patients were in low probability group, one of which was chronic appendicitis, rest 3 was acute appendicitis.

Thus, all appendectomy patients with an AIR score of above 8 had histopathology report positive for appendicitis and majority had an advanced form of appendicitis. In the intermediate group, majority of the patients had earlier stages of appendicitis. Thus, according to all these findings, it can be said that as the stage of appendicitis advances, the AIR score also increases and above 8 AIR score, direct surgical intervention is beneficial.

Chronic appendicitis HPE report was taken as normal and thus the negative appendectomy rate of this study was 10.9%. Of the 6 patients who had a histopathology report of chronic appendicitis, five were in the intermediate group and one in the low probability group according to the AIR score. All had AIR values below 7. These patients could have benefited with a CT evaluation and 6 negative appendectomies could have been avoided.

All conserved patients were followed up for one month to see if there was any recurrence of symptoms and the need for surgery. There were eight patients who developed pain in the lower abdomen again but all were due to causes other than acute appendicitis and none of them required appendectomy. Thus, there was no missed diagnosis of appendicitis in this study.

Andersson M, et al, propose that, Risk-stratification based on a clinical score can be used to optimise the selection of patients for urgent surgical evaluation, diagnostic imaging, in-patient or out-patient observation. In a previous study, the prospective implementation of an algorithm based on the Appendicitis Inflammatory Response (AIR) score led to a reduction in unnecessary hospital admissions and a decreased use of diagnostic imaging.<sup>[13,14]</sup>

Thus, our study suggested, that at a cut off of 7, the AIR score is good at both predicting positive cases and ruling out cases that do not have appendicitis. CT scan to be done in patients with AIR score of 7 and below. Patients with AIR score of 8 and above are unlikely to benefit from CT scan and patients can be directly taken for surgery.

## CONCLUSION

Our study, has shown that AIR score has provided us information regarding patients who need urgent surgery, patients who can be conserved and patients who need further follow-up and evaluation by AIR score or Imaging studies.

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