PREDICTIVE ACCURACY OF MODIFIED ALVARADO SCORE AND APPENDICITIS INFLAMMATORY RESPONSE SCORE (AIR) SCORE IN ACUTE APPENDICITIS

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Abstract

Background: The diagnosis of acute appendicitis, one of the most common causes of acute abdomen till date, still remains a tough one. The decision about its management is complex and it involves surgical procedure utilizing technical, financial and human resources. A quick and accurate diagnosis is extremely important to proceed with an early appendicectomy either to prevent complications or to adopt conservative management to avoid unnecessary negative exploration , which may even lead to increased morbidity.Modifiued Alvarado Score is the commonest scoring system used to diagnose acute appendicitis among several other scoring methods. In the present study we planned to estimate the predictive accuracy of Modified Alvarado Score and a newly developed Appendicitis Inflammatory Response Score (AIR Score)against the reference standard of histopathology in acute appendicitis.

Material & Methods: Data from all patients admitted with a suspected appendicitis and underwent appendicectomy were collected from the case records and their Modified Alvarado Score and AIR score were calculated. Those patients who were treated conservatively were excluded and final diagnosis of appendicitis is confirmed by presence of trans mural inflammatory infiltrate on histopathology of the appendicectomy specimen. Sensitivity, Specificity, Positive Predictive value, Negative predictive Value and Diagnostic Accuracy were calculated for both scores and the predictive accuracy were compared using ROC curves and Area Under the Curve (AUC).

.**Results:** A total of 345 patients were included in this study. Sensitivity,Specificity,Positive Predictive Value ,Negative Predictive Value and Diagnostic Accuracy of Modified Alvarado Score were 70.1%,96.8%,99.5%,24.2% and 72.5% respectively. The newly developed AIR Score showed a Sensitivity of 73.9%, but Specificity and Positive Predictive value100%, Negative Predictive Value of 27.4% and a Diagnostic Accuracy of 76.2%. Kappa statisticsshowed significant higher reliability for AIR Score(0.337) than Modified Alvarado Score (0.284). The predictive validity assessed by AUC was higher for AIR Score (0.987) compared to Modified Alvarado Score (0.956).

Conclusion: Appendicitis Inflammatory Response Score has showed better Predictive Accuracy than Modified Alvarado Score in diagnosing acute appendicitis and can be used as a more reliable tool in the diagnosis of acute appendicitis..

Key words: Acute appendicitis, Modified alvarado score, Appendicitis inflammatory Response score, Predictive accuracy.

BACKGROUND

The diagnosis of one of the most common surgical emergency ,acute appendicitis, still remains a difficult one even with the advent of modern diagnostic tools especially in women. In many countries acute appendicitis is considered a clinical diagnosis by most of the surgeons,

but there is a increased risk of negative laparotomy upto 15-30%.Though newer modalities like Ultrasonography and Computerized Tomography has an effect on reducing the rate even down to 5-10%, the risk of radiation exposure in CT, high cost and delay in obtaining the results in emergency prevents their routine use in clinical practice. Furthermore, if the symptoms are vague, there is delay in clinical diagnosis which cause delayed surgery leading to increased complication like perforation and peritonitis. Many scoring systems like Alvarado Score, Tsanaki Score, and RIPASA Score etc. have been designed to assist in the diagnosis. Among those Alvarado score remains the most simple and widely used one. An ideal scoring system can be used as a tool to speed up and increase the accuracy of decision making thus by reducing the need of potentially harmful and expensive imaging. The limitations of Alvarado score as a diagnostic tool has made it a less reliable scoring system which led to the development of newer scoring systems. Acute Inflammatory Response Score is a newer scoring system which was first used in 2008.

In previous studies, AIR scoring system has been found to outperform Alvarado scoring system as AIR utilizes more objective symptoms than the latter which takes more subjective symptoms like nausea and anorexia in to consideration. AIR score utilizes seven graded parameters including C-reactive protein and these scored variables are used to stratify patients in to low, intermediate and high risk groups.

Cardinal Features of Acute Appendicitis

- Abdominal pain for less than 72 hrs
- Vomiting 1-3 times
- Facial flush
- Tenderness concentrated on the right iliac fossa
- Anterior tenderness on rectal examination
- Fever between 37.3 and 38.5^{0}C
- No evidence of urinary tract infection on urine microscopy

Laboratory Investigations

- CBC : WBC >10,000cells/µL(seen in 80-85% patients), Neutrophilia
- C-Reactive Protein(CRP) :>1mg/dl; Normal CRP level negative predictive value of 97-100%. Very high values with leukocytosis and neutrophilia indicates gangrenous evolution
- Urinary 5-Hydroxy indole acetic acid : significant Increase in acute appendicitis. Decrease in value can be taken as early warning sign of perforation of Appendix
- Liver and Pancreatic function tests.
- Urine analysis to rule out Urinary infections.
- Urine beta-HCG to rule out ectopic pregnancy

Modified Alvarado Scoring system

The Alvarado score was developed in 1986 is a simple additive system to help with the diagnosis of acute appendicitis. It showed a very good sensitivity and specificity when used in western population, but in Asian or Oriental population studies showed limitations of the scoring system. This system uses 8 parameters and stratifies patients into 'appendicitis less likely' , 'probable', and 'acute appendicitis' groups.

Feature	Score
Migration of pain	1
Anorexia	1
Nausea	1
Tenderness right lower quadrant	2
Rebound tenderness	1
Elevated temperature	1
Leukocytosis	2
Shift of WBC count to left	1
Total	**10**

Modified Alvarado scoring system uses seven variables except shift of WBC count to the left making the total score 9 (Kalan,e.al).As mentioned earlier Alvarado scoring system uses more subjective symptoms which can influence the diagnosis. This leads to the development of new scoring system worldwide and the AIR Score is a newer addition to the list.

Appendicitis inflammatory Response (AIR Score)

Appendicitis Inflammation Response Scorewas reported in 2008 by Anderswon and Anderson.It assesses seven graded parameters withatotal score of 12 and accordingly stratifies patients in to a low risk group (0-4), intermediate risk group(5-8) or high risk group (9-12). It uses more objective symptoms and also includes C-reactive protein and is found to outperform Alvarado score in recent studies.

Feature	Score
Vomiting	1
Right iliac fossa pain	1
Rebound tenderness	
Light	1
Moderate	2
Strong	3
Temperature 38.5^{0}C or more	1
White cell count (X10^9/L)	
10-14.9	1
15 or more	2
Proportion of PMNs (%)	
70-84	1
85 or more	2
C-reactive protein (mg/L)	
10-49	1
50 or more	2
Total	**12**
Low risk	**0-4**
Intermediate risk	**5-8**
High risk	**9-12**

MATERIALS AND METHODS

Study Design

Retrospective diagnostic study evaluation

Study Setting And Study Period

Department of General surgery, Government Medical College, Ernakulam from 2016-2019

Study Population

All patients who were admitted with acute appendicitis to general surgical wards in Medical College Hospital Ernakulam and undergone surgical management.

Inclusion criteria

1. Patients admitted with non-traumatic RIF pain of duration 1 week or less,with a suspected diagnosis of acute appendicitis. Suspected appendicitis is defined as acute (<1 week duration) onset non traumatic right iliac fossa pain consistent with a diagnosis of appendicitis, i.e. pain associated with nausea, anorexia, vomiting and fever along with clinical signs as tenderness and rebound tenderness in right iliac fossa.

Exclusion criteria

1. Patients with a history of abdominal trauma
2. Patients with age less than 12 years
3. Abdominal pain of duration more than one week
4. Patients with non RIF pain
5. Patients with other co morbid conditions which could increase the C-reactive protein.

Methodology

All patients who were admitted with suspected signs and symptoms of acute appendicitisand undergone appendicectomy will be included in the present study. The case records will be collected from the Records library. The data will be collected in a proforma by the investigator from each case sheet. The proforma contains all the study variables including demographic, clinical and laboratory data and both modified Alvarado score and AIR score will be calculated for each patient by the investigator.

The final diagnosis of appendicitis will be based on histologic examination of the appendix showing transmuralneutrophilic infiltrate.

Patients were classified as having non appendicitis pain if they underwentnegative exploration which is defined as the absence of transmuralneutrophilic

Infiltrate on histologic examination of the appendix.

STATISTICAL ANALYSIS

Sample Size Calculation

Sample size will be calculated for sensitivity and specificity for each test and the sum will be taken as the total sample size for each diagnostic score. Higher sample size is taken for the study purpose.

$$n_{(total)} = n_{(sen)} + n_{(spe)}$$

Sensitivity and Specificity of Modified Alavarado(MAS) is 94% and 90% respectively (previous studies)

Sensitivity and Specificity of AIR score is 96.5%and 90% respectively

$$n_{(sen)} = \frac{TP+FN}{P}$$ P= Prevalence of acute appendicitis (7%)

$$TP+FN = Z^2 \frac{sensitivity*(1-sensitivity)}{d^2}$$ Z=1.96   d=10%

$$n_{(spe)} = \frac{TN+FP}{1-P}$$

$$TN+FP = Z^2 \frac{specificity*(1-specificity)}{d^2}$$

Sample size is estimated to be 345for MAS and sample size for AIR is 196. Since 345 is higher it is taken as the study sample size.

RESULTS

Total no.of patients included in the study was 351, out of which 320(91.2%) confirmed to have acute appendicitis by Positive HPE and 31 have negative HPE results.(Table 1).

Table 1. Histopathology

Histopathology	No. of patients	Percentage
No	31	8.8
Yes	320	91.2

Distribution of patients according to age group showed majority of the patients belonged to the <29yrs of age group.(Table 2).

Table 2.Distribution of patients according to Age groups

Age	Sex				Total
	Female		Male		
	n	%	n	%	
<20	54	39.7	82	60.3	136
20-29	27	21.4	99	78.6	126
30-39	20	46.5	23	53.5	43
40-49	18	54.5	15	45.5	33
>50	6	46.2	7	53.8	13
Total	125	35.6	226	64.4	351

Total no of males and females participated in the study were 226 and 125 respectively. Out of the 226 males 200 and out of 125 females 120 were diagnosed having acute appendicitis by positive HPE (Table 3).

Table 3.Distribution of patients according to Sex

SEX	Histopathology				Total
	NO		YES		
	n	%	n	%	
Female	5	4	120	96	125
Male	26	11.5	200	88.5	226
Total	31		320		351

The analysis of CRP values, an important objective variable used in the calculation of AIR Score showed the following results. It was <10 in 16 patients, out of which 7 cases turned out to be positive for acute appendicitis. In 231 cases CRP values were >50 out of which, 227 patients diagnosed to have the disease. This association between positive HPE and increased CRP values was found to be statistically significant with a p value <0.001. (Table 4)

Table 4. CRP Values

CRP Value	Histopathology				Total
	Yes		No		
	n	%	N	%	
<10	7	43.8	9	56.3	16
10-49	86	82.7	18	17.3	104
≥50	227	98.3	4	1.7	231
Total	320	91.2	31	8.8	351

X^2 value= 68.42, p-value <0.001

Modified Alvarado Score and AIR Score were calculated in all 351 patients using the observations in the study. MAS predicted 227 out of 351 patients as having acute appendicitis out of which 225 (99.6%) turned out to be having the same by histopathology. Only one patient (0.4%) who was predicted as having appendicitis did turn out to be of negative HPE. (Table 5)

Table 5. Modified Alvarado Score

MAS	Histopathology				Total
	Yes		No		
	n	%	N	%	
<7	94	75.8	30	24.2	124
≥7	225	99.6	1	0.4	226
Total	319	91.1	31	8.9	350

X^2 value= 55.95, p-value <0.001

Out of 351 patients, AIR Score identified 237 patients as having increased risk for acute appendicitis of which all 237 were proven by HPE. (Table 6).

Table 6. Appendicitis Inflammatory Response Score

AIR	Histopathology				Total
	Yes		No		
	n	%	N	%	
<9	83	72.8	31	27.2	114
≥9	237	100	0	0	237
Total	320	91.2	31	8.8	351

X^2 value= 70.69, p-value <0.001

The sensitivity, specificity, Positive predictive value, negative predictive value and accuracy for MAS and AIRS are 94%, 87%, 99%, 59%, 93.42% and 95%, 97%, 100%, 65%, 95.16% respectively. ROC curve

analysis of MAS showed a cut of value of 4.5, while that of AIRS was 6.5. The predictive validity of both Modified Alvarado Score and AIR Score was assessed by the Area under ROC curve (AUC) and found to be higher for AIRS (0.988) compared to that of MAS (0.956). (Table 7, 8, 9, 10, 11, 12,13,14) (Figure 1, 2).

Table 7

Area Under the Curve of MAS			
Area	p-value	95% CI	
0.956	<0.001	0.922	0.991

Table 8

	Modified Alvorado Score		
CUT OFF	Sensitivity	Specificity	Yudens J
0.00	1.00	0.00	0.00
1.50	1.00	0.06	0.06
2.50	1.00	0.13	0.13
3.50	0.98	0.65	0.63
4.50	0.94	0.87	0.81
5.50	0.85	0.94	0.79
6.50	0.71	0.97	0.67
7.50	0.35	1.00	0.35
12.50	0.00	1.00	0.00
18.00	0.00	1.00	0.00

Cut off value 4.5

Table 9

	Cut off = 4.5
Sensitivity	94%
Specificity	87%
PPV	99%
NPV	59%
Accuracy	93.42%

Table 10

Area Under the Curve of AIR Score			
Area	p-value	95% CI	
0.988	<0.001	0.978	0.998

Table 11

CUT OFF	AIR Score		
	Sensitivity	Specificity	yudens J
1.00	1.00	0.00	0.00
2.50	1.00	0.03	0.03
3.50	1.00	0.06	0.06
4.50	0.99	0.42	0.41
5.50	0.99	0.74	0.74
6.50	0.95	0.97	0.92
7.50	0.87	1.00	0.87
8.50	0.74	1.00	0.74
9.50	0.58	1.00	0.58
10.50	0.35	1.00	0.35
11.50	0.13	1.00	0.13
15.00	0.00	1.00	0.00
19.00	0.00	1.00	0.00

Table12

	Cut off = 6.5
Sensitivity	95%
Specificity	97%
PPV	100%
NPV	65%
Accuracy	95.16%

Table13. Area under Curve

	AUC	SE[a]	95%CI[b]	p
AIR_Score	0.988	0.0048	0970 to 0.996	<0.001
Modified_Alvarado_Score	0.956	0.0172	0.929 to 0.975	<0.001

Table 14.Pair wise comparison of ROC curves

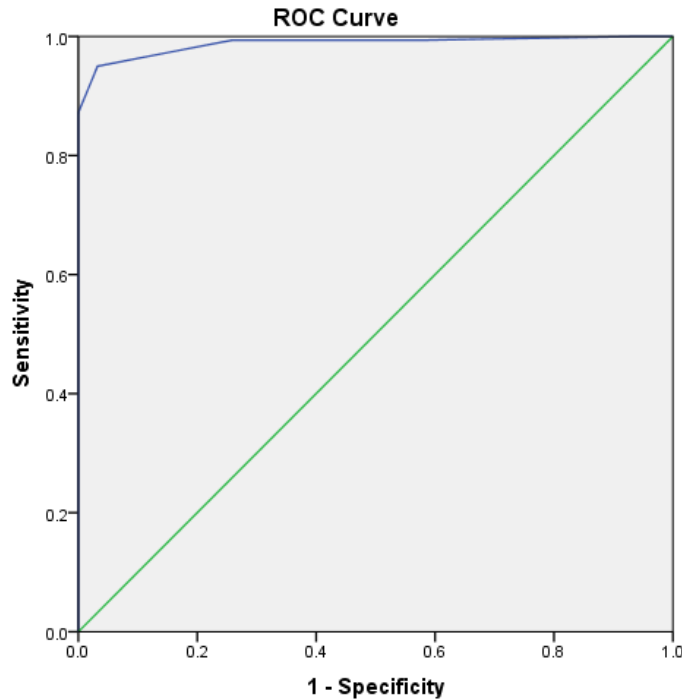| AIR_Score- Modified_Alvarado_Score	
Difference between areas	0.0313
Standard Error	0.016
95% Confidence Interval	-0.000532 to 0.0632
z statistic	1.927
Significance Level	P=0.0539
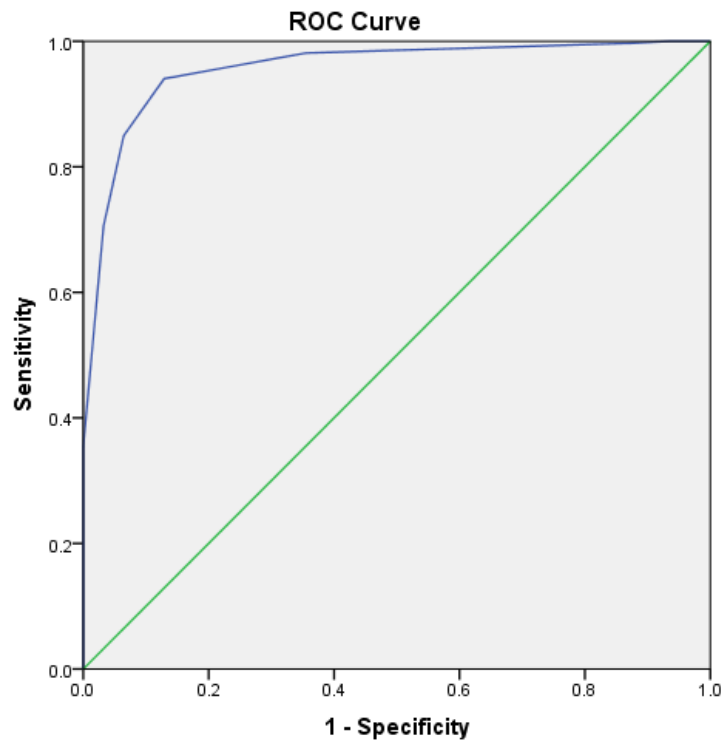
Figure 1 : ROC of MAS

Figure 2 : ROC of AIR Score

DISCUSSION

Being a very difficult entity to diagnose, the decision for conservative management of acute appendicitis is routinely taken by Modified Alvarado Scoring system in almost all institutions. Recently many newer scoring systems claim superiority over Alvarado Score, AIR score being one of them. In the present study we compared the predictive accuracy of AIR Score with Modified Alvarado Score in diagnosing acute appendicitis. Histopathology (HPE) of appendicectomy specimen was taken as the gold standard for confirmation of diagnosis.

A total of 351 patients were included in the study. 91.2% (n=320) were confirmed to have acute appendicitis by positive histopathology and 8.8 %(n=31) were negative for acute appendicitis. This observation is in consensus with previous studies which showed a negative appendicectomy rates between 7% and 12 %.[11] Majority of the patients were in the Age Group less than 30 years which is in agreement with previous studies by OmariAH,et.al. stating that acute appendicitis is a disease of young age with only 10-15% cases occurring in the elderly.[12] Hence a better diagnostic tool can reduce the negative appendicectomy rate and the potential morbidity and mortality resulting from a operative procedure mainly in the young adult population.

In this study, Modified Alvarado Score predicted 226 patients out of the 345 as having acute appendicitis out of which 225(99.6%) turned out to be having the same by histopathology. Only one patient (0.4%) who was predicted as having appendicitis did turn out to be of negative histopathology.

Out of the 124 patients who had MAS of less than 7, 30 patients had no appendicitis and 94 patients had appendicitis. The sensitivity and specificity of the test were calculated as 94% and 87% respectively. The positive predictive value was high (99%).A study by Emmanuel S, et al showed a sensitivity of 94.1 % and 90% respectively for MAS which is close to the current study. The diagnostic Accuracyof present study is 93.42% which is consistent with the above study(92.9%).Sensitivity and Specificity of Alvarado Score according to another study by Madasi. V, et.al [10] were 87.3% and 52.4% respectively, and had a

diagnostic accuracy of 85%.Several other studies showed the sensitivity and specificity of MAS between 85% to 95% and diagnostic accuracy above 90%.

Out of the total 345 patients, AIR score identified 237patients as having high risk for acute appendicitis of which all 232 were proven by histopathology. Sensitivity of AIR score was calculated to be 95% which is almost equal to that of MAS,but it had a specificity of 100% compared to the 87% of MAS. Out of the total 124 patients who had AIR score less than 9, 31 patients had no appendicitis by histology. Hence a positive Predictive Value of 100% and a NegativePredictive Value of 27.4% were obtained.The diagnostic Accuracy of AIR score is 76.2% according to the study.In a similar study by Madasi.V, et.al, the sensitivity and specificity were 95.7% and 90.5% respectively.

The reliability of the risk scores as measured by kappa statistics was considerably higher for AIR score (0.337) than Modified Alvarado Score (0.284) which was statistically significant (p value <0.001). According to the present study, the Positive Predictive Value and Diagnostic Accuracy for AIR score are considerably higher than those for Modified Alvarado Score and were statistically significant.

On pair wise comparison of AIR score and Modified Alvarado Score, the difference between areas was 0.016 with significance level of p = 0.053.

On comparison of both scores by plotting ROC curve and Area Under the Curve (AUC), AIR score had AUC of 0.987 and Modified Alvarado Score had AUC of 0.956 which were of statistical significance (P value <0.001). Madasi. V, et.al [10] plotted AUC of 0.95 for AIR score and 0.74 for Modified Alvarado Score. Andersson, M. and R. E. Andersson[8], who whileproposing the AIR score have reported an ROC area of 0.93 for AIR score and0.88 for Modified Alvarado Score in appendicitis.

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