# Alvarado Score Still Holds: A Prospective Comparison of Modified Alvarado Score [MAS] and Appendicitis Inflammatory Response Score [AIRS] as a Diagnostic Aid in Acute Appendicitis

Varun Kumar Singh<sup>1</sup>, Bikram Kharga<sup>2</sup>, Kumar Nishant<sup>2</sup>, Phuchungla Bhutia<sup>1</sup>, Barun Kumar Sharma<sup>3</sup>, Neha Pandey<sup>4</sup>.

<sup>1</sup>Assistant Professor, Department of Surgery. <sup>2</sup>Associate Professor, Department of Surgery. <sup>3</sup>Associate Professor, Department of Radiodiagnosis. <sup>4</sup>MBBS – Undergraduate Student. All authors are from Sikkim Manipal Institute of Medical Sciences, Gangtok, India

Address for Correspondence: Varun Kumar Singh, Department of Surgery, Sikkim Manipal Institute of Medical Sciences, 5<sup>th</sup> Mile, Tadong, Gangtok, Sikkim. India. Mail Id: varunsingh.vks@gmail.com

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### Abstract

**Introduction:** In pre-imaging era, diagnosis of appendicitis was based on clinical assessment. To decrease chances of error and negative appendectomy, Alvarado was first to propose a score in 1885. A number of scores were then put forward including modification of Alvarado score. This study aimed to compare two most commonly used systems, MAS and AIRS. **Methods:** On admission MAS and AIRS were compared in patients of right iliac fossa pain who subsequently underwent appendectomy. Histopathologic examination was taken as gold standard outcome and MAS and AIRS as tests under evaluation. **Results:** Study analysed 229 patients with a mean age of 32.69 years and male to female ratio of 1.04. Female patients were older than male patients [35.25 and 30.14 years, respectively; p=0.017]. Negative appendectomy rate was just under 4%. Sensitivity, specificity, PPV and NPV of MAS were 85%, 44.4%, 97.4% and 10.8% and for AIRS were 81.8%, 11.1%, 95.7% and 2.4%. Sensitivity in children and adolescents was 90% and 72.5% for MAS and AIRS, respectively. There was no gender difference between the two. AUC for ROC curve of MAS and AIRS was 0.669 [0.474-0.863] and 0.481 [0.285-0.677] with a significant difference [p=0.0003]. **Conclusion:** Both scores are sensitive, underdiagnose patients as low risk, but don't leave any patient with advanced appendicitis. MAS outperforms AIRS for all cases of appendicitis as well as advanced appendicitis. Since both scores classify a large number of patients as low risk, before deciding a surgical intervention, an imaging aid should always be welcome.

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Key words- AIRS, Alvarado, Appendicitis, Appendectomy, MAS

### Introduction

The diagnosis of acute appendicitis, the most common surgical abdominal emergency [<sup>i</sup>] has been a clinical quandary and continues to be so. Though the rate of incorrect diagnoses has come down with the advent of high end diagnostic modalities like ultrasonography and computed tomography, the surprises continue to pop up even now [<sup>ii</sup>].

Manuscript Received: 24<sup>th</sup> August 2016 Reviewed: 6<sup>th</sup> September 2016 Author Corrected: 18<sup>th</sup> September 2016 Accepted for Publication: 30<sup>th</sup> September 2016 It is not uncommon to have a decision making dilemma, whether or not to explore a patient even after imaging work up, when the literature still documents a negative appendectomy rate somewhere between 15-34% [<sup>iii</sup>,<sup>iv</sup>]. And therefore, finally it rests on clinical acumen. Various scores [which include clinical, biochemical, their combinations and emphasis on repeated examinations] have been proposed and compared to each other over and again but to no avail [<sup>v</sup>, <sup>vi</sup>, <sup>vii</sup>, <sup>viii</sup>]. Most common scores in use are original Alvarado score [OAS] and its modification [MAS] and Appendicitis Inflammatory

Response Score [AIRS]. This study has tried to examine the status of MAS and AIRS in the ethnic population of Sikkim, a north east state of India.

# **Patients and Methods**

A prospective observational analytic study was planned to evaluate and compare the on admission Modified Alvarado Score [MAS] and Appendicitis Inflammatory Response Score [AIRS] in patients of right iliac fossa pain, in whom an appendicular pathology was suspected.

The intra-operative findings and post-operative histopathology of the specimen were then compared to MAS and AIRS.

The study was conducted in Sikkim Manipal Institute of Medical Sciences in Gangtok, the capital town of Sikkim, one of the north east states of India and lasted over a duration of 2 years from April 2013 to March 2015. Patients of all age groups were included provided they underwent appendectomy in the institution. There were no major exclusions except a mismatch in recording of data. Histopathological examination was taken as the gold standard outcome and MAS and AIRS as tests under evaluation.

The recording of data [of MAS and AIRS] was designed in such a way so that each of the scores were recorded by two surgeons independently [*Table 1*]. Thus there were 4 surgeons, two of them recorded MAS and two recorded AIRS.

Any mismatch in data recorded by the two surgeons was a criteria kept for exclusion. Data was tabulated and analysed using IBM<sup>©</sup> SPSS<sup>©</sup> 20.0 and Microsoft<sup>©</sup> Excel<sup>©</sup> 2013.

### Results

Over a study duration of 2 years, 267 patients underwent surgery for an indication of appendicular pathology in the institute. After carefully scrutinizing recorded data, 38 patients who had a mismatch in entries recorded by the two surgeons independently, were excluded.

Thus, data of 229 patients was analysed after the end of the study. Of these 229 patients, 226 patients underwent appendectomy and 3 patients had the intra-operative diagnosis of perforated Meckel's diverticulum and were regarded as negative appendectomies while analysing the data.

Male patients marginally outnumbered female patients by a male to female ratio of 1.04. The mean age of the study population was 32.69 years. Most of the patients were young as half of the patients [50.3%] were in  $3^{rd}$  and  $4^{th}$  decade of life. Children and adolescents formed 23.2% of total cases.

The distribution of male and female patients across age groups was a significant observation as the sex ratio reversed from that in favour of males to that of females as the age advanced. Consequently female patients had a higher mean age [35.35 years] compared to male counterparts [30.14 years] [df=1, F=5.819, p=0.017] [*Table 2*].

Out of 226 histopathologic examinations, 185 patients had a diagnosis of acute appendicitis and 20 patients had acute on chronic appendicitis. Number of patients with chronic appendicitis was 10 and 5 patients had acute eosinophilic appendicitis. There were 6 patients [2.6%] who had usual histology of normal appendix. Three patients had perforation of Meckel's diverticulum. Thus there were 9 [3.9%] negative appendectomies [*Table 3*].

MAS predicted high likelihood of appendicitis in 94 patients [41%] while the score remained indeterminate or borderline in 98 patients [42.8%]. There were 37 patients [16.2%] in whom MAS was 4 or less thus almost excluding the possibility of appendicitis.

Comparing the data with histopathology of the appendix specimen, MAS could truly predict the least possibility of appendicitis in 4 out of 6 patients while in remaining 2 patients the score was borderline. However, in those 94 patients in whom MAS predicted high likelihood of appendicitis, final histology was appendicitis [*Table 3*].

Compared to MAS [41%], AIRS could definitely predict AIRS in 34 patients [14.8%]. The score was borderline in almost two thirds of patients [67.2%]. However, the number of patients in whom AIRS predicted least likelihood of appendicitis was comparable to MAS [41 (17.9%) and 37 (16.2%) for MAS and AIRS, respectively].

Out of 6 patients with final histology of normal appendix, AIRS could predict least possibility of appendicitis in 1 patient, and 5 patients had a preoperative diagnosis of borderline appendicitis. In those 34 patients in whom AIRS predicted definitive appendicitis, no patient was found to have a negative report of appendicitis [*Table 3*].

Mean MAS and AIRS of the patients was 6.20 [out of 9] and 6.24 [out of 12], respectively, both in the borderline range. The value of both MAS and AIRS was lower for male patients [6.02 and 6.19, respectively], compared to female patients [6.38 and 6.29 respectively]. However, the difference of mean MAS and mean AIRS between the two genders was not significant [p=0.076 and 0.699, respectively] concluding both the score predict the probability of appendicitis in a similar way between the two genders.

When the MAS and AIRS were compared independently among the various age groups, we found the scores to be more predictable in middle age group patients compared to those in immediate younger and older age groups. However, predictability again increased in extremes of ages [p<0.001] [*Table 4, Figure 1*].

Mean percentage scores of MAS and AIRS were 68.85 and 51.96, respectively [df=228, t=15.13, p<0.001]. For the same patient, MAS could achieve a higher score compared to AIRS and therefore predicted the possibility of appendicitis in a more definite way.

Parameters		MAS	AIRS	
Symptoms	Migratory RIF pain	1	1	
	Anorexia	1		
	Nausea/ vomiting	1	1	
Signs	Tenderness RIF	2		
	Rebound tenderness in RIF	1	1 [Mild]	
			2 [Moderate]	
			3 [Severe]	
	Elevated temperature	1	1	
Investigations	Leucocytosis	$2 [\geq 10 \times 10^3 / \text{ cumm}]$	$1 [10x10^{3}-14.9x10^{3}/ \text{ cumm}]$	
			$2 [\geq 15 \times 10^{3} / \text{ cumm}]$	
	Polymorphs		1 [70-84%]	
			2 [≥85%]	
	CRP		1 [1-4.9 mg/l]	
			2 [≥5 mg/l]	
Total		0-9	0-12	
	Interpretation	0-4 Low probability	0-4 Low probability	
		5-7 Borderline/ Equivocal	5-8 Borderline/ Equivocal	
		8-9 High probability	9-12 High probability	

### Table-1: Comparison between MAS and AIRS

### Mean AIRS Ν Mean MAS Age Group Total Female Overall Overall Male Female Male Male Female 0-10 7 6 13 7.43 7.67 7.54 7.00 8.00 7.46 11-20 24 16 40 6.29 6.25 6.28 6.50 5.50 6.10 21-30 41 26 67 5.63 5.62 5.63 5.63 5.38 5.54 31-40 22 26 48 5.64 6.69 6.21 6.18 7.04 6.65 41-50 12 19 31 7.00 6.89 6.94 6.50 6.79 6.68 9 51-60 15 7.83 7.44 7.60 6 5.17 6.33 5.87 61-70 5.00 3 5 8 5.67 5.80 5.75 5.00 5.00 71-80 1 3 4 6.00 6.00 6.00 4.00 4.00 4.00 2 81-90 1 1 8.00 6.00 7.00 8.00 4.00 6.00 0 8.00 ≥91 1 1 8.00 8.00 8.00 ----Total 117 112 229 6.02 6.38 6.20 6.19 6.29 6.24

### Table-2: Patients' distribution across their age and gender along with mean MAS and AIRS

### Table-3: Final Histopathology and MAS and AIRS stratification across diagnosis

Scoring	Score and		Арре	Normal	Total		
System	Probability	Acute	Acute on chronic	Chronic	Acute Eosinophilic	Histology	
Ν		185	20	10	5	6+3*	229
MAS	0-4 Low	24	7	1	1	4+1*	38
	5-7 Borderline	84	2	6	3	2+2*	99
	8-9 High	77	11	3	1	0	92
AIRS	0-4 Low	39	0	1	0	1	41
	5-8 Borderline	115	20	9	4	5+1*	154
	9-12 High	31	0	0	1	0+2*	34
*3 Patients had Meckel's diverticulum perforation and were regarded as negative appendectomies.							

### Table-4: Binary Classifiers at cut-off 5 for MAS and AIRS in male, female and paediatric patients\*

Scoring	Gender	Sensitivity	Specificity	PPV	NPV	LR+	LR-
System							
MAS	Male	82.9	50	96.8	13.6	1.66	0.34
	Female	87.2	33.3	97.9	6.7	1.31	0.38
	Children*‡	90		97.3			
AIRS	Male†	84.7		94			
	Female	78.9	33.3	97.7	4.2	1.18	0.63
	Children*‡	72.5		96.7		0.7	

\*Include children and adolescents, †AIRS failed to stratify any of the male patients as low risk who didn't have appendicitis [True Negatives=0], ‡Both MAS and AIRS couldn't detect those children who didn't have appendicitis [True Negatives=0]

### Table-5: Binary Classifiers at different cut-offs for MAS and AIRS

Cut-off	Scoring	Sensitivity	Specificity	PPV	NPV	LR+	LR-
Value	System						
5	MAS	85.0	44.4	97.4	10.8	1.5	0.3
	AIRS	81.8	11.1	95.7	2.4	0.9	1.6
6	MAS	62.7	66.7	97.9	6.8	1.9	0.6
	AIRS	58.6	44.4	96.3	4.2	1.1	0.9
7	MAS	41.8	77.8	97.9	5.2	1.9	0.7
	AIRS	45.9	66.7	97.1	4.8	1.4	0.8
8	MAS	23.6	88.9	98.1	4.5	2.1	0.9
	AIRS	30.0	66.7	95.7	3.8	0.9	1.0
9	MAS	10.5	100	100	4.4		0.9
	AIRS	14.5	77.8	94.1	3.6	0.7	1.1

Bold fonts indicate the lower and higher cut-offs for MAS and AIRS, respectively. The final comparison between MAS and AIRS has been done at cut-off 5 [for both] for lower threshold and at cut-off 8 for MAS and 9 for AIRS.

Figures









At the borderline cut-off value of 5, both MAS and AIRS were highly sensitive [85% and 81.8%, respectively], however, MAS was much more specific compared to AIRS [44.4% and 11.1%, respectively]. As the cut-off values are increased, sensitivity of both the scoring systems decline sharply. At the defined cut-off for high probability of appendicitis for both the systems [8 for MAS and 9 for AIRS], MAS remained more sensitive and specific compared to AIRS, though the sensitivity was too low compared to cut-off of 5. Positive predictive value of MAS improved while that of AIRS declined on increasing the value of cut-off, even though the value remained above 94% of both the scores at all cut-offs [*Table 5*]. The area under curve [AUC] for receiver operating characteristic [ROC] curves for MAS was 0.689 [95% CI: 0.506-0.872] and for AIRS was 0.481 [0.285-0.677] with statistically significant difference [p=0.0003]. The curve of AIRS is dipped twice below reference line indicating the utility of AIRS as a diagnostic tool in appendicitis is very poor [*Figure 2*].

### Discussion

Taking a call for operative intervention in non-traumatic acute abdomen is not easy especially when there is limited access to imaging in an emergency set up. The bulk of these cases are acute appendicitis. Over the study duration of 2 years, 3,285 patients of all age groups were admitted with complaints of either right lower abdomen pain or poorly localized/ diffuse lower abdomen pain in surgery ward. Of these, 267 patients underwent appendectomy constituting 8.13% of the total population of patients presenting with some symptoms suspicious of appendicitis.

Pouget-Baudry reviewed the role of OAS in management of right lower quadrant pain and found a score of less than 4 was associated with absence of appendicitis while more than 6 was significantly associated with acute appendicitis [<sup>ix</sup>]. In a retrospective study [n=155], done in our institute in 2010, Dey et al [including the authors of this study] concluded OAS could be an easy, simple, effective and cheap alternative to imaging modalities which are not readily available in developed countries.

Overall sensitivity and specificity were 94.2% and 70% with a PPV of 86.9% and NPV of 69.8% [<sup>x</sup>]. Denizbasi found the sensitivity and specificity of OAS to be 95.4% and 45%, respectively [<sup>xi</sup>]. We used MAS rather than OAS in our study and its sensitivity and specificity were less [85%, 44.4%, respectively]. Minimum MAS score in our study was 4 and no patient had a score less than that. Ozkan et al in his retrospective study found sensitivity, specificity, PPV and NPV of OAS were 54%, 73.3%, 88.2% and 29.7%, respectively with a significant difference between the two genders [sensitivity=64.3%, 28.6%; specificity 57.1%, 75%; PPV=90%, 66.7% and NPV=21.1%, 37.5%, respectively for men and women] [<sup>xii</sup>]. Denizbasi also found significant gender difference in PPV [p=0.045] and NPV [p=0.02] [11].

However, we didn't find any difference between the mean percentage scores of two genders [p=0.176 and 0.117, respectively for MAS and AIRS].

In Ebell's systematic review of 28 prospective studies, LR+ for OAS in adults were 0.03, 0.42 and 3.4 for cutoffs <4, 4-6 and >6, respectively and 0.01, 0.98 and 6.7 for cut-offs <5, 5-8 and >8, respectively. Similarly, the values for children were 0.02, 0.27, 4.2 [for <4, 4-6, >6] and 0.04, 1.2, 8.5 [for <5, 5-8, >8]. Overall LR+ in our study was 1.5 for a cut-off for 5, 1.9 for cut-off of 6 and 7 and 2.1 for a cut-off 8 in case of MAS. In case of AIRS the LR+ was highest [1.4] for cut-off of 7 [<sup>xiii</sup>]. Golden et al [n=287] found OAS had a positive likelihood ratio [LR+] of 2.2 [95% CI: 1.7-3] and negative likelihood ratio [LR-] of 0.6 [0.4-0.7]. Similar values for MAS were 2.4 [1.6-3.4] and 0.7 [0.6-0.8] [<sup>xiv</sup>]. The LR+ in present study was 1.5 and 0.9 for MAS and AIRS, respectively while the LR- was 0.3 and 1.6.

In Ohle's systematic review of 42 studies related to the OAS in predicting appendicitis, he found the OAS to be a useful diagnostic tool in ruling out acute appendicitis at a cut-off of 5 for all patient groups. He also concluded that the score works well in male patients but is inconsistent in children and tends to over predict appendicitis in female patients. In our study, MAS was better than AIRS in ruling out appendicitis as MAS predicted 5 [55.55%] patients as low risk out of 9 patients with final negative histology [including three patients with intra-operative diagnosis of Meckel's diverticulum] but AIRS could predict only 1 [11.11%] patient as low risk. In children MAS was 90% sensitive compared to overall sensitivity of 85% but the sensitivity of AIRS was lower compared to overall sensitivity [72.5% and 81.8%, respectively]. However, both the MAS and AIRS predicted the only child with negative histology as low risk [xv]. Bundy, in

his meta-analysis of 42 level 3 articles, concluded OAS and MAS worked best in older age groups. Chances of appendicitis rose to 4 fold if the score was 7 or more [LR=4.0 for OAS and 3.6 for MAS] and dipped to  $4/5^{\text{th}}$  if it was less than 7 [LR=0.20 for OAS and 0.30 for MAS]. In our study MAS had an overall LR (+) of 1.9 for a cut-off of 7 and 2.1 for a cut-off of 8 [<sup>xvi</sup>].

Ohmann did a prospective interventional [before and after trial] study [n=1484] where he compared a group of standard diagnostic workup without any additional diagnostic support with a group of patients undergoing additional diagnostic support with a score and concluded that the integration of a clinical score in the diagnostic process cannot be recommended as a standard diagnostic tool for decision making in acute appendicitis [xvii].

Scott et al calculated AIRS during a 50 week prospective study [n=464] and found 63.3% patients had low risk, however 6.2% of them had appendicitis. In contrast we had 17.9% patients classified as low risk through AIRS but almost all of them except one had appendicitis on final histology. Sensitivity and specificity were 90% [cut-off 5] and 98% [cut-off 9], respective values in our study were 81.8% and 77.8% [xviii].

Chong et al compared OAS and RIPASA score derived from 192 patients with right iliac fossa pains and found OAS to be less sensitive for Asian population. The sensitivity of OAS [cut-off 7] and RIPASA score [cut-off 7.5] were 68.3% and 98%, respectively, while at a similar cut-off of 7, the MAS was just 41.8% sensitive and AIRS was 45.9%. However, the comparison was between a 10 point score [MAS] and 17.5 point score [RIPASA] at almost a similar cut-off [7 and 7.5, respectively] and at a cut-off of 5, MAS, though still lagging, is not far behind RIPASA score in our study [<sup>xix</sup>].

Kollar et al compared AIRS, OAS and initial impression of a senior surgeon and found all methods stratified similar proportions [~40%] of patients to low risk [p=0.233] with a false negative rate [FNR] of <8%. While MAS and AIRS in our study could stratify 16.15% and 17.9% patients to low risk [p=0.309] with an FNR of 15% and 18.2%, respectively. AIRS assigned a much smaller proportion to high risk patients compared to OAS [14 and 45%, respectively] in his study. Similarly AIRS identified 14.8% and MAS 41% patients as high risk [p<0.001]. In

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contrast to Kollar's finding of higher specificity and PPV of AIRS [97% and 88%, respectively] compared to OAS [76% and 65%, respectively], our AIRS was less specific and had a lower PPV [77.8% and 94.1%, respectively] compared to MAS [88.9% vs 98.1%] [<sup>xx</sup>].

Sammalkorpi et al developed a new adult appendicitis score and prospectively compared it to OAS and AIRS. OAS outperformed the rest in terms of sensitivity, but the specificity and LR were better in the new score as well as AIRS. The AUC of new score was 0.882 [0.858-0.906] and of OAS and AIRS was 0.790 [0.758-0.823] and 0.810 [0.779-0.840] [<sup>xxi</sup>]. In Andersson's prospective study [n=545], AIRS outperformed OAS. AUC for AIRS was 0.93 for all cases of appendicitis compared to 0.88 for OAS [p=0.0007], the values for advanced appendicitis were 0.97 and 0.92, respectively [p=0.0027] [<sup>xxii</sup>].

Golden found AUC for MAS was 0.7 and was not significantly different from that in OAS [0.72], physician determined likelihood [0.72] or RIPASA score [0.67] [14]. deCastro plotted ROC curves in a prospective study [n=941, 346 had appendicular pathology] and AUC was greater for AIRS [0.96 for AIRS, 0.82 for OAS, p<0.05] [<sup>xxiii</sup>]. In contrast, MAS outperformed AIRS in our study with values of AUC for MAC was 0.669 and for AIRS was 0.438 [p=0.0003].

## Conclusion

Both MAS and AIRS are quite sensitive at lower threshold but underdiagnose a fair number of patients as low risk, even when they have appendicitis but don't leave any patient with advanced appendicitis even at a higher threshold. However, MAS outperforms AIRS in most of the parameters for both all cases of appendicitis as well as advanced appendicitis. Both the scores are more predictable in middle age and in extremes of age and can be used in children and old age patients with similar predictability. Since both scores classify a large number of patients as low risk, before deciding a surgical intervention, an imaging aid should always be welcome.

**Limitation-** We took final histopathology as the gold standard for diagnosis of appendicitis. So those patients who couldn't undergo appendectomy but probably had appendicitis, were excluded from the study thus decreasing the false negatives.

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### Conflict of Interests-None

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