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# Accuracy of Diagnostic Scales of Acute Appendicitis: Alvarado, RIPASA and AIR in Comparison to Histopathology

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***Original Article***

## Abstract

***Background****: Different diagnostic tools are utilized for diagnosis of appendicitis. Alvarado, RIPASA and AIR scales among the commonly used diagnostic scoring systems. Many studies compared these scales against histopathology, but few studies compared the three scales at the same time.*

***Objective****: To compare and evaluate the performance of these three scales against histopathology.*

***Methods****:*

*During a period of three years, a total of 328 Iraqi patients who were presented with signs and symptoms of acute appendicitis and to whom appendectomy was performed. Confirmation of the diagnosis of acute appendicitis by histopathology study as a gold standard. Preoperative assessment of the patients with the three diagnostic scales was conducted and the scores for each diagnostic scale was reported and compared. A score of ≥ 7 or higher on Alvarado scale, a score of ≥ 7.5 on RIPASA and a score of ≥ 5 on AIR scale were considered as cutoff points for high risk or probability of acute appendicitis (positive test).*

***Results****:*

*By receiver operating characteristics (ROC) curve analysis using the standard cutoff points Alvarado scale showed a sensitivity, specificity and diagnostic accuracy, of 80.3%, 73.2% and 79.9%, respectively, the corresponding values for RIPASA scale were, 96.1%, 90.9% and 95.4% and for AIR scale they were, 88.4%, 77.3%, 86%,, respectively.*

***Conclusions****: Alvarado, RIPASA and AIR scales were good predictors to detect correctly the high risk of acute appendicitis with a high sensitivity, good specificity and high positive predictive values. RIPASA scale showed better diagnostic performance than the other two scales while Alvarado and AIR were not much different.*

***Keywords****: Acute appendicitis, diagnosis, histopathology, diagnostic scales, accuracy*

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## 1. INTRODUCTION

Acute appendicitis (AA) is a common surgical disease and most frequently causes hospitalization and emergency surgery; in 2019, there were about 18 million cases of AA with an incidence rate of almost 230 per 100,000 population. The incidence rate continue to increase, since 1990 the rate increased by almost 39% in 2019. The mortality rate due to AA and its complication is about 0.43/100,000 with over than 33400 deaths reported in 2019. Acute appendicitis commonly occur between the age 10-20 years with a peak incidence in the age 15-19 years with a life time risk of 8.6% in males and 6.7% in females (1,2).

The causes of appendicitis are varied and not well recognized, however, it could be associated with bacterial infection, in particular Escherichia coli, Bacteroides, Klebsiella, Clostridia, which are more common cultured bacteria in AA cases, viruses and other microorganisms are not uncommonly contribute to AA, infection with Enterobius Vermicularis is also suggested as a risk factor for AA (3–5).

Currently, there is no generally accepted theory to explain pathogenesis of AA, there are various pathogenetic events contribute to AA in majority of patients, the primary stage is obstruction of the lumen which could be contributed to different sources such as fecaliths, hyperplasia of lymphatic tissue, parasites, foreign body or tumor metastasis, At the second stage, the visceral afferent thoracic nerves (8th-10th) are stimulated leading to mild periumbilical pain which often last for almost 6 hours, later on when the intraluminal pressure increases it leads to arterial insufficiency which causes a reduction in the perfusion of the appendiceal wall and further cause ischemic changes in the tissues and compromise the mucosa. After this stage bacterial invasion into the luminal wall causing transmural inflammation which extended further than appendix at this stage the inflammation of the adjacent structures and parietal peritoneum occur lead to more severe pain, and usually accompanied by anorexia, nausea, vomiting and fever (6). However, a new concept in the etiopathogenesis of AA suggested microbiological, molecular, immunological and biochemical pathogenetic role (7). Many classifications of AA have been proposed, which are based on morphological changes in the appendix and features of the clinical course of the disease Simple (catarrhal, superficial)-non-destructive and destructive that include phlegmonous, gangrenous and mixed forms of destructive appendicitis (4,8).

There are variety of clinical features of acute appendicitis, these features determined by the location of the appendix in the abdominal cavity; severity of destructive changes in the appendix; the duration of the disease; age, sex, presence of concomitant diseases; the presence of complications. Acute appendicitis could be presented with typical presentation with vague periumbilical pain lasting for more than a few hours , later migrate to the right iliac fossa and often be accompanied by nausea /vomiting and loss of appetite, in some patients the temperature can reach 38-39 °, and sometimes even higher. (9) sometimes, presentation is atypical and the initial complaint is right lower quadrant pain(10).

Although there is a long period of time since the first description of AA, it is still sometimes represents a diagnostic problem and a challenge for all surgeons and physicians who care for patients with suggestive symptoms despite their experience and availability of different clinical and diagnostic methods. Some difficulty to reach the definite diagnosis, especially in young, elderly and women of reproductive age, (11–13) where various gynecological and reproductive inflammatory diseases can present with similar signs and symptoms and have to be excluded(14).

Appendectomy is currently the most common emergency surgical procedure in the world, it is performed either laparoscopically or by conventional open appendectomy (15). However, in patients with acute appendicitis, a delay in performing appendectomy to improve diagnostic accuracy increases the risk of appendicular perforation and sepsis, as well as morbidity and mortality, in contrast, the lower diagnostic accuracy will lead to unnecessary appendectomies with a signifciant negative appendectomy rate of about 20%-40% however, controversy still exist regarding the timing of appendectomy (16–18)

Currently, several clinical scores are available for the diagnosis of acute appendicitis however, they are different in their validity and accuracy (16,19,20),. Combination of these tools may improve the accuracy of diagnosis and reduce the negative appendectomies (21). Several scales like Alvarado, Raja Isteri Pengiran Anak Saleha Hospital (RIPASA), and Appendicitis Inflammatory Response (AIR) score (22) that include the classical signs and symptoms of acute appendicitis plus laboratory studies have been developed and used worldwide. The Alvarado scale (Table 1) is the best known and the one that until a few years ago showed the best performance in validation studies (23). It was developed in 1986 by Dr. Alfredo

Alvarado(24). The AIR score (Table 2) is a scoring system, created in Sweden in 2008, developed by Andersson and Andersson (22). Later, the RIPASA scale (Table 3) has been released at the Raja Isteri Pengiran Anak Saleha Hospital (RIPASA), by Chong, et al. (25,26); This scale was developed in Asia in 2010, so its applicability and effectiveness in other populations is still under study. However, despite clinical assessment remain the cornerstone, histopathology is the reference and the gold standard for diagnosis, validity of different diagnostic scales and other tools have to be validated against histopathology, therefore we aimed in this study to assess the validity of three diagnostic scales that are widely applicable in our practice; Alvarado, RIPASA and AIR scales as diagnostic tool for acute appendicitis. We aimed also to assess the combination of two or more of these scales and investigate the improvement in the diagnostic ability of these scales separately and combined, and to assess the ability to get more accurate and precise diagnostic tool.

**Table 1. Alvarado score** (27)

| **Variables** | **Clinical features** | **Score** |
|---|---|---|
| Symptoms | Migratory RIF pain | **1** |
| | Anorexia | **1** |
| | Nausea and vomiting | **1** |
| Signs | Tenderness RIF | **2** |
| | Rebound tenderness | **1** |
| | Elevated temperature | **1** |
| Laboratory | Leucocytosis | **2** |
| | Shift to left | **1** |
| **Total Score** | | **10** |

**Score of 0 – 4** : low risk; there is a very low probability of appendicitis.
**Score of 5 – 6:** Intermediate risk; the patient has probable appendicitis and serial clinical and laboratory evaluations will be required, as well as some imaging studies (ultrasonography, computed tomography).
**Score of ≥ 7:** High risk of acute appendicitis and requires surgery

**Table 2. AIR scale (28)**

| Diagnosis | | score |
|---|---|---|
| Vomiting | | 1 |
| Pain in Right Iliac Fossa | | 1 |
| Abdominal Defense | low | 1 |
| | Mild | 2 |
| | Severe | 3 |
| Temperature >38,5 °C | | 1 |
| Neutrophils | 70-84% | 1 |
| | >85% | 2 |
| Leukocytes | >10.0-14.9 x 109/l | 1 |
| | >15.0 x 109/l | 2 |
| C - reactive protein | 10-49 g/l | 1 |
| | >50 g/l | 2 |

Total AIR score = 0-4: low probability of appendicitis.

Total AIR score = 5-8 mild probability of appendicitis.

Total AIR score = 9-12: high probability of appendicitis.

**Table 3. RIPASA scale** (25)

| Criteria | | Score |
|---|---|---|
| 1. Demography | Female | 0.5 |
| | Male | 1 |
| | Age < 40 years | 1 |
| | Age > 40 years | 0.5 |
| 2 Symptoms | Right Iliac Fossa | 0.5 |
| | Pain migration to RIF | 0.5 |
| | Anorexia | 1 |
| | Nausea & vomiting | 1 |
| | Duration of symptoms <48 hrs. | 1 |
| | Duration of symptoms >48 hrs. | 0.5 |
| 3. Signs | Right Iliac Fossa tenderness | 1 |
| | Guarding | 2 |
| | Rebound tenderness | 1 |
| | Rovsing sign | 2 |
| | Fever >37° C <39° C | 1 |
| 4. Investigation | Raised white blood cell counts | 1 |
| | Negative urine analysis | 1 |
| 5 Additional score | Non-Asian | 1 |

| | | |
|---|---|---|
| Total score | < 5 | less likely |
| | 5.0 – 7.0 | Low probability |
| | 7.5 – 11 | High probability |
| | > 12 | Refer to surgery for appendectomy |

## 2. PATIENTS and METHODS

This was an observational prospective comparative study carried out during a period of 3 years where 328 cases admitted to the emergency department with abdominal pain and typical signs and symptoms that were suggestive of acute appendicitis. Patients who met the inclusion criteria were enrolled in the study.

**Inclusion criteria**

1. Adult patients aged 18 years or above
2. Both genders
3. Admitted to the emergency department with typical features suggestive of acute appendicitis.
4. Signed the informed consent for operation and participation in the study.

**Exclusion criteria**

1. Patient with a known cause of abdominal pain other than acute appendicitis.
2. Pregnant women.
3. Previous urolithiasis
4. Pelvic inflammatory disease
5. Voluntary discharge before completing the protocol of diagnosis

**Study protocol and Diagnostic confirmation**

Preoperatively, full history was taken and thorough clinical examination was performed to reach the clinical diagnosis.

In all patients included in the study the Alvarado, AIR and RIPASA scales were applied. When the diagnosis approved clinically and by the diagnostic scales, patients were operated on with standard procedure of appendectomy under general anesthesia. The excised appendix then sent for histopathology study and the histopathological results were reported.

Postoperatively, all patients were admitted to the surgical ward, put under observation, appropriate prophylactic antibiotics and analgesic agents were prescribed.

All patients were followed up to assess any complication or adverse outcome, then patients discharged home.

Confirmation of the diagnosis of acute appendicitis by histopathology study as a gold standard (Reference method).

Acute appendicitis cases were defined when the patients presented with non-traumatic right iliac fossa pain lasting for less than 4 days and undergoing emergency appendectomy for suspected appendicitis (29).

A score of ≥ 7 or higher on Alvarado scale, a score of ≥ 7.5 on RIPASA and a score of ≥ 5 on AIR scale were considered as cutoff points for high risk or probability of acute appendicitis (positive test).

**Sample size and Statistical analysis:**

Sample size for the study was calculated using the standard equation for the diagnostic tests studies with a power of 80% and alpha error of 5%. Data were analyzed using the Statistical Package for Social Sciences. (SPSS) version 26. Descriptive statistics were performed with measures of central tendency; mean, median, range, standard deviation, frequencies and percentages for the general data. Analysis of diagnostic validity parameters (sensitivity, specificity, predictive values and accuracy) using frequency distribution and cross-tabulation to assess each scale against the "gold standard", Histopathology. Further assessment was performed using Receiver Operating Characteristics (ROC) curve to assess the validity parameters for each scale against histopathology, area under the ROC curve (AUC) was calculated which is an estimator of the validity of a diagnostic test; AUC of less than 0.6 indicated failed diagnostic ability of a test, AUC of 0.6 to 0.7 indicates fair validity, 0.8-0.9 good validity and >0.9 excellent validity. Youden's index used to determine the optimal cutoff point for each scale. Additionally, agreement between the three scales was assessed with modified Kappa analysis . Level of significance set at 0.05 or less to be significant.

## 3. RESULTS

A total of 328 patients were enrolled in this study with a mean age 24.6 ± 8.3 years. The age distribution of the studied group revealed that 43% of the patients were younger than 20 years, 29% at the age 21-30 years and the remaining patients were older than 30 years. Males were relatively dominant,179/328 with a male to female ratio of 1.2 to one. Most patients, 76.2% of urban origin. Normal body mass index found in 39.3%, overweight patients were 37.2% and obese patients were 77 (23.5%). Regarding the surgical approach, Laparoscopic appendectomy performed in 237 (72.3%) while open appendectomy in 91 (27.7%), (**Table 4**).

Preoperative laboratory findings of the studied group are summarized in (**Table 5**).

Histopathological examination of the appendectomy specimens revealed that out of the 328 specimens, appendicitis documented in 284 (86.6%) giving a negative appendectomy rate of 13.4%.

The results of scores reported by each scale were compared to histopathology as a gold standard reference method.

When Alvarado scale was applied, a total of 238 patients (72.6%) had high risk of appendicitis with a score of ≥ 7, among them the histopathological finding was positive in 228 (95.8%) and negative in 10 (4.2%) on the other hand, there were 90 (27.4%%) patients with low/intermediate risk (score <7), among them the histopathological finding was positive in 56 (62.2%). and negative in 34 (37.8%), (**Table 6**).

The RIPASA scale revealed that 277 (84.5%) patients with high probability (a score of ≥ 7.5) and 15.5% with low probability of appendicitis (score < 7.5).

Histopathological finding was positive in 273 (98.6%) and negative in 11 (21.6%); Among the 51 (15.5%) patients with low probability, the histopathological finding was positive in 11 (21.6%) and negative in 40 (78.4%). Collecting all the data, there were 273 true positives, 4 patients with positive scale and negative histopathological study, 40 true negatives and 11 patients with negative scale and positive histopathological study, (**Table 7**).

The AIR scale was positive (score ≥ 5, high probability) in 261 patients (79.6%) among them histopathological finding was positive in 251 (96.2%) and negative in 10 (3.8%). Among the 67 cases with negative AIR (score < 5) of low probability, histopathological study was positive in33 (49.3%) and negative in 34 (50.7%); In total, the true positive cases were 251 and the true negative cases were 34, (**Table 8**).

Further analysis was performed using the receiver operating characteristics (ROC) curve (Figure 2) to assess the validity and performance of the three scales in comparison to histopathology. We used a score of 7 as cutoff point for Alvarado, a score of 7.5 for RIPASA and a score of 5 for AIR scale. ROC curve analysis revealed that at these cutoff points, Alvarado scale had an area under the curve (AUC) of 0.776, sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV) and negative predictive value (NPV) of 80.3%, 73.2%, 79.9%, 95.8% and 37.8%, respectively.

RIPASA scale showed an AUC of 0.940 and sensitivity, specificity, diagnostic accuracy, PPV and NPV of 96.1%, 90.9%, 95.4%, 98.6% and 78.4%, respectively.

AIR scale showed an AUC of 0.790 and sensitivity, specificity, diagnostic accuracy, PPV and NPV of 88.4%, 77.3%, 86%, 95.1% and 48.4%, respectively.

By comparing these validity parameters, RIPASA scale had the better performance and diagnostic accuracy compared to the other two scales. Additionally, AIR scale was relatively better than Alvarado scale, (**Table 9**).

Table 4. Baseline characteristics of the studied group (N=328)

| Variable | | No. | % |
|---|---|---|---|
| Age | < 20 | 141 | 43.0 |
| | 21 - 30 | 95 | 29.0 |
| | 31 - 40 | 64 | 19.5 |
| | > 40 | 28 | 8.5 |
| | Mean(SD) | 24.4 (8.3) | - |
| Gender | Male | 179 | 54.6 |
| | Female | 149 | 45.4 |
| | M:F ratio | 1.20 | - |
| Residence | Urban | 250 | 76.2 |
| | Rural | 78 | 23.8 |
| BMI | Normal | 129 | 39.3 |
| | Overweight | 122 | 37.2 |
| | Obese | 77 | 23.5 |
| | Mean(SD) | 27.1 (5.3) | - |
| Surgical approach | Laparoscopic | 237 | 72.3 |
| | Open | 91 | 27.7 |
| SD: standard deviation, M:F ratio male to female ratio | | | |

Table 5. Laboratory findings of the studied group

| Parameter | Mean | SD | Range |
|---|---|---|---|
| WBC | 13.4 | 2.1 | 3.6 - 22.7 |
| Neutrophil | 9.6 | 1.7 | 1.2 - 18.4 |
| Lymphocyte | 2.3 | 0.4 | 0.9 - 10.6 |
| Thrombocyte | 258 | 39.1 | 118 - 522 |
| MPV | 8.5 | 1.3 | 6.2 - 14.1 |
| RDW | 12.5 | 1.9 | 8.4 - 19.6 |

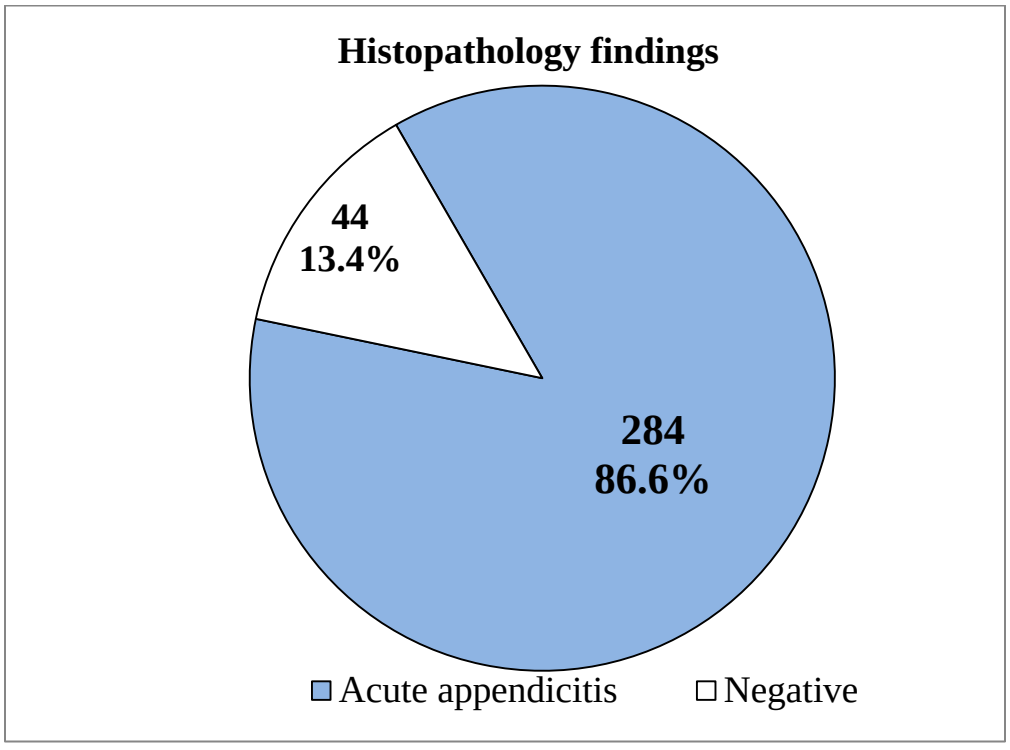


Figure 1. Distribution of the studied group according to the Histopathology study

Table 6. Cross-tabulation for Alvarado scale and histopathology

| Alvarado | Histopathology | | | | Total | |
|---|---|---|---|---|---|---|
| | Acute appendicitis | | negative | | | |
| | No. | % | No. | % | No. | % |
| ≥ 7 | 228 | 95.8 | 10 | 4.2 | 238 | 72.6 |
| < 7 | 56 | 62.2 | 34 | 37.8 | 90 | 27.4 |
| Total | 284 | 86.6 | 44 | 13.4 | 328 | 100.0 |

Table 7. Cross-tabulation for RIPASA scale and histopathology

| RIPASA | Histopathology | | | | Total | |
|---|---|---|---|---|---|---|
| | Acute appendicitis | | negative | | | |
| | No. | % | No. | % | No. | % |
| ≥ 7.5 | 273 | 98.6 | 4 | 1.4 | 277 | 84.5 |
| < 7.5 | 11 | 21.6 | 40 | 78.4 | 51 | 15.5 |
| Total | 284 | 86.6 | 44 | 13.4 | 328 | 100.0 |

Table 8. Cross-tabulation for AIR scale and histopathology

| AIR scale | Histopathology | | | | Total | |
|---|---|---|---|---|---|---|
| | Acute appendicitis | | negative | | | |
| | No. | % | No. | % | No. | % |
| ≥ 5 | 251 | 96.2 | 10 | 3.8 | 261 | 79.6 |
| < 5 | 33 | 49.3 | 34 | 50.7 | 67 | 20.4 |
| Total | 284 | 86.6 | 44 | 13.4 | 328 | 100.0 |

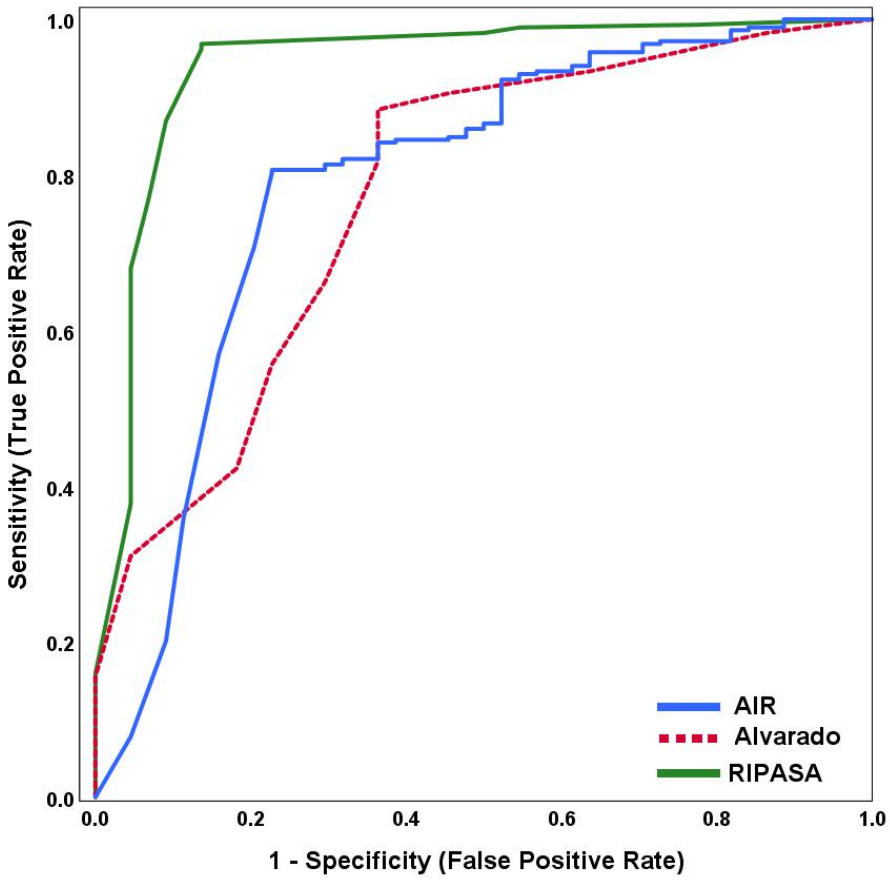


Figure 2. Reciever operating characteristics (ROC) curve for the performance of the three scoring systems

Table 9. Validity parameters of the three diagnostic scales

| | **Alvarado scale** | **RIPASA scale** | **AIR scale** | **P. value** |
|---|---|---|---|---|
| Cutoff point | ≥7 | ≥ 7.5 | ≥ 5 | - |
| AUC | 0.776 | **0.940** | 0.790 | **0.002** |
| Sensitivity | 80.3% | 96.1% | 88.4% | **0.018** |
| Specificity | 73.2% | 90.9% | 77.3% | **0.013** |
| Accuracy | 79.9% | 95.4% | 86.0% | **0.035** |
| PPV | 95.8% | 98.6% | 95.1% | 0.192 ns |
| NPV | 37.8% | 78.4% | 48.4% | **0.004** |
| PPV : positive predictive value, NPV: negative predictive value, ns: not significant | | | | |

## 4. DISCUSSION

Appendicitis remains one of the commonest abdominal surgical emergency faced by surgeon on daily practice worldwide (30). Different diagnostic tools are utilized to get more precise diagnosis that support the clinical decision and rule out those with low risk particularly in pediatric group (31), however, histopathology is the gold standard for diagnosis (32,33). Despite the emergence of different diagnostic scales, there still some drawback in the diagnostic accuracy of some scales and a considerable negative appendectomy rates have been documented in almost all centers, therefore, improving the performance of these scales continues and new diagnostic scales are adopted for optimization and improvement of diagnostic performance of the current scales (34–36). Alvarado, RIPASA and AIR scales among the commonly used diagnostic scoring scales. Many studies compared these scales against histopathology, but few studies compared the three scales at the same time (16,22,25,28,37), therefore, the present study aimed to compare these three diagnostic scales against each other and histopathology to evaluate their performance and validity among group of Iraqi patients. Hence, a total of 328 Iraqi patients presented with signs and symptoms of acute appendicitis and admitted to the emergency department and operated on were enrolled in this study. In our study, the demographic characteristics of the patients were consistent with epidemiological picture of appendicitis cases with regard to the incidence by age and gender where majority of our patients of were young adults with predominance in males in a ratio of 1.2 to one. Similar to previous national and international studies (30,38,39)

As already described, our study is the first that compare these three diagnostic scales, however, there are numerous that compare Alvarado and AIR, or Alvarado and RIPASA. Comparing our results with those available in the other literature, we find that in the studies of Andersson and Andersson (40) as far as AIR and Alvarado are concerned there is a complete contrast, but the study by Sammalkorpi, et al. (41) shows similarity with ours in terms of specificity, with better sensitivity for ours, comparing AIR and Alvarado. Studies carried out by Aydin et al. (21) in 2017, Gopalam et al. in 2017, Umar et al. in 2020 Jose and Rajesh (22) in 2021 and Bouali et al. in 2022 (27), present results similar to those found for the Alvarado scale in the present study, sharing results with the world literature.

As far as diagnostic accuracy is concerned, we obtained 79.9% diagnostic accuracy for

Alvarado, 95.4% for RIPASA compared to 86% for AIR, having almost similar values to those available in the literature (16,22,24,25,27,37). Moreover, some authors documented that RIPASA and AIR are superior to Alvarado scales as we found in our study (29,29,42)

On the same subject, Walczak, et al.(43) in their study that included 92 patients who underwent laparotomy on suspicion of acute appendicitis compared five different scales including RIPASA and Alvarado. They concluded that most of the systems used showed high sensitivity and positive predictive value, allowing truly positive cases to be selected and reduced unnecessary laparotomies. On the other hand, there is evidence of low specificity and negative predictive value, which could be associated with late diagnosis and subsequent complications. These results differ from those of the rest of the literature, particularly with regard to specificity. Our positive predictive value was high for the three scales, but we got low negative predictive values. However, further studies are still needed for more precise evaluation.

## 5. CONCLUSIONS

We conclude in this study that the Alvarado, RIPASA and AIR scales were good predictors to detect correctly the high risk of acute appendicitis with a high sensitivity, good specificity and high PPV. RIPASA scale showed better diagnostic performance than the other two scales while Alvarado and AIR were not much different. However, screening for the preoperative diagnosis of patients with suspected acute appendicitis continues to be challenging. Although its diagnosis is considered relatively easy, the classic signs of appendicitis can sometimes be difficult to obtain and are only unequivocally present. This study sought to determine which scale has greater precision as a diagnostic test, obtaining more precision with the RIPASA scale. This can be applied to our population as an objective method to support decision about management of suspected cases of appendicitis.

Regarding the rate of negative appendectomies, we firmly believe that we are within an acceptable range (13.4%) and that we will focus more on short-term follow-up of suspected patients

**Ethical Clearance:**

Ethical issues were approved by the authors and study was approved by the research ethics committee. Informed consent was obtained from each participant. Data collection was in accordance with the World Medical Association (WMA) declaration of Helsinki for the Ethical Principles for Medical Research Involving Human Subjects, 2013 and all information and privacy of participants were kept confidentially.

**Conflict of interest:** Authors declared none

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